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TREATMENT OF RELAPSED, RESISTANT AND NEGLECTED CONGENITAL TALIPES EQUINO-VARUS.[1]

By LENNOX G. TEECE,

Sydney.

THE first essential is to define clearly the title of my address lest in discussion we find ourselves at cross-purposes. For the purpose of this address I exclude from the categories of relapsed, resistant and neglected congenital *talipes equino-varus* children who have not as yet walked, and in point of fact the vast majority of the children with whom I propose to deal fall within the age group three to ten years.

In these days the completely neglected condition is rare. Practically all the children have had some treatment of varying degrees of efficiency. They may have had a gradual correction with zinc oxide adhesive and a strap and buckle, which in many cases takes complete care of the correction of the deformity, with the unfortunate exception in a number of instances of the inward tilt of the *os calcis*. Successive encasement in plaster of Paris, with or without wrenching under an anæsthetic, may have been employed. In some cases correction may have been attempted by the application of a Denis Browne splint. Resort may have been had to multiple tenotomies combined with wrenching under an anæsthetic. It is not always fair to state that the patients have been resistant to the above-mentioned methods of correction without inquiring closely into the method of their application. Lack of adequate supervision and the allocation of the treatment to inexperienced persons may nullify the value of any method. These patients above all require the close personal attention of the surgeon.

The condition falls into the resistant class only when the above-mentioned lines of treatment have failed after being studiously and persistently pursued. Relapse of the condition is only too common, and when it occurs blame is not necessarily to be attached either to the surgeon or to the mother. Some patients, in spite of constant supervision and in spite of prolonged plaster immobilization after full correction has been obtained, will repeatedly show signs of relapse within a short period of removal of the retentive apparatus. In this address I concern myself with the class of patient in whose treatment the above-mentioned routine methods have failed, or who have relapsed after correction has been obtained and who have been walking for at least some months.

Our ideal objective is obviously complete permanent correction of each element of the deformity combined with full mobility of all joints. The minimum with which we should be satisfied is a plantigrade foot with an absence of equinus deformity. The main elements of deformity in order of increasing importance are adduction of the fore-

[1] President's address, delivered at the annual meeting of the Australian Orthopædic Association, Hobart, September 9 to 12, 1953.

foot, the inward tilt of the heel and the equinus deformity. The adduction of the forefoot is the least important factor and its persistence is not inconsistent with the attainment of a plantigrade foot and normal function. This is a fortunate fact, because in the class of patient with whom I am dealing it can often be corrected only by an extensive and unwarranted bone operation, mobility being sacrificed for the sake of appearance. The patients under present consideration need operation—soft tissue or bony or both. Operations on the tarsal bones are to be reserved for those patients in whom growth in the deformed attitude has led to actual alteration in the shape of the bony components of the foot. Prior to such an occurrence, adequate division or stripping of resistant and shortened soft tissue structures will produce correction.

The chief resistant structures are the *tibialis posticus* tendon and sometimes the tendon of the *flexor longus digitorum*, the internal lateral or deltoid ligament of the ankle, the spring ligament, the interosseous talo-calcanean ligament and the *tendo Achillis*, though here, as always, the correction of the equinus deformity must be left to the last and usually performed as a second-stage operation. Many names are associated with the development of the operative correction of *talipes equino-varus*, but with the soft tissue group of operative procedures the name of Ober, of Boston, is the one most closely associated.

When the medial side of the ankle joint and foot are exposed by incision, the taut nature of the ligaments is at once apparent, and their successive division leads step by step to correction of the deformity. The *tibialis posterior* tendon is divided early, and it is important to detach all the fibres of the internal lateral ligament from the medial malleolus. Some of these fibres are deeply attached beneath the tip of the malleolus. Continuing forwards, the talo-navicular and navicular cuneiform joints must be opened and the dorsal ligaments pushed laterally and the spring ligament freed and pushed down into the sole of the foot, special care being taken to remove it from its attachment to the navicular. When we have proceeded thus far, the inward tilt of the heel remains unaltered, and the crucial part of the operation is the next step, which consists of complete and careful division of the interosseous talo-calcanean ligament, whereupon the *os calcis* can be swung outwards on the talus. Even in the younger children it is remarkable to observe the wide gap which ensues between the head of the talus and the navicular and the contiguous medial aspects of the talus and the *os calcis*. Nearly always the correction of the equinus deformity should be left to a later stage.

The post-operative swelling after this procedure is often extreme, and in many cases it is wise to place the foot in a plaster cast in only partial correction. If the deformity has been of a high grade and the foot is placed in full correction, the posterior tibial artery will be unduly stretched. In my earlier cases, when I put the foot up in full correction I had on some occasions in the next seventy-two hours to split the plaster cast from end to end because of embarrassment of the circulation, thereby losing a large part of the correction. It is better to place the foot in the mid-position instead of in the valgus position, and three weeks later to change the plaster cast. At the same time the *tendo Achillis* can be divided and the equinus deformity corrected. Plaster fixation should be continued in all for a period of three months, and after its removal an inside iron and an outside "T" strap should be employed for some months, relatively inefficient though they may be. This procedure, which leaves untouched the bones and the articular surfaces, provides a foot of nearly normal mobility. It does not always completely correct the relatively minor element of the adduction of the forefoot. The prognosis as regards subsequent further relapse depends on the peronei muscles. Until they show adequate voluntary power, in every case there is danger of a relapse. After the removal of the plaster the child must be trained to exercise the peronei muscles.

Only too often one encounters patients in whom attack on the ligamentous and tendinous structures is insufficient to correct deformity. In the course of growth which has taken place in the deformed attitude, alteration has occurred in the actual shape of the bony components of the foot. Most important is the fact that, in the growing foot which has been long maintained in the position of equinus, the broad front part of the body of the talus will no longer fit into the tibio-fibular socket, so that even after division of the *tendo Achillis* dorsiflexion of the foot, even to the right angle, is impossible. There is in addition actual alteration in shape of the tarsal bones. Correction in some cases can be obtained only by the sacrifice of mobility. The tarsus must be stabilized by arthrodesis as the first step and secondarily the equinus deformity corrected, though both procedures can be carried out at the same time.

In correcting the bony deformity of the tarsus, the blind wedge exsection has long since been outmoded. It used to consist of removal of a wedge of bone base laterally from the tarsus, sufficient to correct the varus generally without regard to the joints through which it passed. At the same time it had no corrective influence on the inward tilt of the heel.

All tarsal arthrodeses, for whatever purpose performed, are based on the same principles and differ only in detail. They all commence by dividing the tarsus into three parts—namely, the talus, the *os calcis*, and the rest of the tarsus. An arthrodesis is produced in the calcaneo-cuboid, talo-navicular and talo-calcanean joints. A wedge is removed, based laterally from the calcaneo-cuboid joint, including the articular surface of both bones. The articular cartilage is removed from the contiguous surfaces of the talus and navicular. This procedure takes care of the adduction element of the deformity. The removal of a wedge, based laterally from the talo-calcanean joint, corrects the inward tilt of the heel.

Experience shows that after this operation fusion of the talo-calcanean and the calcaneo-cuboid joints takes place rapidly, but that fusion of the talo-navicular joint is often long delayed. At this stage the equinus deformity is still left, and this is the most important and the most difficult to correct. Division of the *tendo Achillis* and of the posterior capsule of the ankle joint advances us little if at all. There is a disproportion in size between the body of the talus and the tibio-fibular socket which must contain it. It is possible to narrow the body of the talus by removal of a slice from its lateral aspect in the sagittal plane, but this is not to be recommended. In a young child it will not result in ankylosis of the ankle, but it will cause considerable limitation of movement. It is better to enlarge the tibio-fibular socket. It has often been recommended that this should be effected by prising apart the distal ends of the tibia and fibula, but it is not possible to do this to an appreciable extent in the presence of an intact interosseous membrane. Separate, as best you may, the lower ends of the tibia and fibula; but it is my practice in addition to divide the fibular shaft just above the malleolus. One then forces the lateral malleolus outwards, producing in effect the deformity of a Pott's or abduction fracture. The socket must by these means be sufficiently widened to hold the body of the talus readily and to permit dorsiflexion to within the right angle. Post-operative immobilization in plaster of Paris must be continued for three months, by which time a sufficient degree of tarsal fusion should be present to permit of unprotected weight-bearing. It should be an invariable rule to change the plaster cast at the end of two or three weeks, at which time the stitches are removed. An anæsthetic should be administered so that, if necessary, any remodelling of the position can be carried out before the new close-fitting unpadded plaster cast is applied.

Whether the equino-varus deformity is one which has been corrected primarily without operative interference or whether it is a late untreated or relapsed deformity requiring operative correction, I believe in keeping the patient under supervision till he has reached the age of ten years, or alternatively for five years after the final correction of the deformity, whichever period be the longer. This may necessitate only six monthly visits to the surgeon, and is a precaution well worth while.

In the past we have been too readily satisfied with our results, especially when we have not insisted on a meticulous follow-up of our patients. Patients who relapse—and this is particularly true of public hospital patients—tend to go somewhere else; and, indeed, in children's hospitals they are often turned out at the age of twelve years and told to go somewhere else—a most reprehensible practice. Let us therefore cling to our own patients over an adequate follow-up period. We shall then no longer rest content in the smug belief that all our own patients are permanently cured, even though we expend considerable time in the treatment of the relapsed patients of our colleagues.

DELAYED UNION AND NON-UNION IN FRACTURES OF THE SHAFT OF THE FEMUR.[1]

By W. D. STURROCK,
Sydney.

THIS short paper is presented to show the method of treatment for fractures of the shaft of the femur which either have failed to unite or in which it was considered union had been delayed sufficiently to warrant operative treatment. It is probably correct to state that some of the fractured femurs included in the delayed union series would have united if rest had been followed for a sufficiently long time. However, prolonged splinting for periods of up to nine or twelve months usually results in a very restricted range of knee movements, and it has been in an endeavour to prevent this unfortunate sequela of fractured femurs that conservatism has not been followed beyond a certain period.

Failure of the fracture to proceed to early union has been found in the majority of cases to be due to the interposition of soft tissue between the fracture ends. This is invariably accompanied by only "fair" reduction, as seen in the post-reduction X-ray films. In many cases so-called distraction of the fracture ends is due not to excessive weight used in traction, but to muscle which prevents the ends of the bone coming together. Occasionally union is delayed or fails to occur for no readily explainable reason. In two cases in which a transverse fracture of the mid-shaft occurred, reduction by conservative means was good, but union failed to occur and examination of a section of the bone sent was reported to reveal changes suggestive of early Paget's disease. The time since operation has been too short to confirm this diagnosis.

Delayed union in the femur is very common when the fracture is accompanied by a fracture of the tibia on the same side. In this series of cases delayed union is considered to be present when at the end of ten weeks there is free mobility at the fracture site and there is minimal or no radiological evidence of callus formation.

The patients in this series have all been treated by the same methods since January, 1950. The patient is placed on the traction table, which is tilted so that the injured limb can be approached readily from the postero-lateral aspect. A long incision is made over the postero-lateral aspect of the thigh, and the femur is approached by lifting up the *vastus lateralis* muscle from the lateral intermuscular septum. After the fractured ends have been freed, a V-shaped wedge is cut to expose the medullary cavity in each fragment, the medial or posterior cortex of the fracture being left untouched so that no loss of length is incurred. In delayed union the amount of bone removed is small, and in non-union the amount of bone removed is extensive. For delayed union a long plate is then fixed by at least six screws over the lateral aspect of the femur. In cases of non-union a long, broad tibial graft consisting of the whole width of the subcutaneous surface of the tibia, and preferably nine to ten inches long, is fixed by four screws over the lateral aspect of the femur. The V-shaped gap in the femur itself is then packed tightly with soft cancellous bone which has been taken from the ilium.

In two cases of grossly comminuted fracture of the shaft of the femur, in which the comminution extended for a distance of six to eight inches, iliac bone chips were used to pack in and around the fragments without any internal fixation. In two cases only, after a wedge section from the femur had been excised, an intramedullary nail was used; but this method of treatment is not recommended, as union does not always appear to proceed to consolidation. Post-operative treatment consists of immobilizing the limb in a Thomas splint. Clinical and radiological union is usually firm at the end of about two months, and the traction is then changed to the method of Hamilton Russell, when knee movements can be instituted. If the fractured femur is accompanied by a fractured tibia, then pin traction through the upper end of the tibia after internal fixation of the femur is used instead of skin traction.

Fourteen patients with delayed union of a fracture of the femur have been treated by the method described, and in no case has union not been sufficiently firm to allow weight-bearing within eighteen weeks. Eleven patients with established non-union of a fracture of the femur have been treated by the method described, and again union has occurred in every case within a period of eighteen weeks, except in one case, in which an intramedullary nail was used when union was still not complete radiologically eighteen months after operation.

[1] Read at the annual meeting of the Australian Orthopædic Association, Hobart, September 9 to 12, 1953.

OSTEOPOROSIS.[1]

By E. F. WEST,
Adelaide.

OSTEOPOROSIS is defined in "Gould's Medical Dictionary" (fifth edition, 1941) as "an enlargement of the spaces of bone, whereby a porous appearance is produced".

Adult bone is normally subject to two continuous processes, formation and resorption. The mass of bone may be deficient, either because resorption is too great (hyperparathyroidism with *osteitis fibrosa generalisata*) or because formation is too little (osteoporosis and osteomalacia). Formation of bone may be too little, furthermore, either because the osteoblasts do not lay down sufficient osseous matrix or because the matrix, once laid down, is not calcified. The former condition is osteoporosis, the latter osteomalacia or rickets.

Several forms of osteoporosis are recognized (Snapper, 1949). If insufficient protein is ingested during starvation, insufficient bone matrix is manufactured and "hunger osteoporosis" results. In the post-menopausal period the protein metabolism is interfered with; the formation of the matrix may be impaired and post-menopausal osteoporosis may result. A similar process in old age leads to senile osteoporosis. Faulty protein metabolism is a characteristic feature in Cushing's syndrome, and in this disease, too, osteoporosis is frequent. Finally, immobilization paralyses the activity of the osteoblasts because their function is stimulated by normal stresses and strains. Thus during the inactivity caused by a plaster cast or paralysis, the osteoblastic function diminishes; no bone matrix is manufactured and osteoporosis of disuse results.

Since osteoporosis is due to faulty deposition of protein-rich bone matrix, it is not a disease primarily connected with a disturbance of calcium metabolism. Serum calcium, phosphorus and phosphatase values are therefore normal in osteoporosis.

Conditions associated with Osteoporosis.

The following are conditions associated with osteoporosis: (i) starvation, due to insufficient protein being

[1] Read at the annual meeting of the Australian Orthopædic Association, Hobart, September 9 to 12, 1953.

ingested; (ii) immobilization: lack of normal stresses and strains depresesses osteoblastic activity; (iii) the post-menopausal state: deficiency of œstrogens results in depression of osteoblastic activity; (iv) senility: depression of osteoblastic activity is part of the general slowing up of metabolism—all tissues atrophy; (v) Cushing's syndrome, in which an excess of the adrenal cortical "sugar" or "S" hormone inhibits anabolism of protoplasm, including bone matrix; (vi) acromegaly, in which the cause may be the increase of pituitary hormone or the secondary lack of gonadal hormones; (vii) unknown cause—the idiopathic type.

The three common types of osteoporosis met with in orthopædic practice are senile osteoporosis, post-menopausal osteoporosis, and the osteoporosis of immobilization. Fuller Albright (1941), in reporting 40 cases of post-menopausal osteoporosis, found that the average time of onset after the menopause was nine and a half years in the 27 cases of uncomplicated physiological menopause, and thirten and two-fifth years in the 10 cases of artificial menopause.

All writers agree that among older people osteoporosis occurs much more frequently in women than in men. The relationship is about four to one. Osteoporosis in patients aged between forty and sixty years occurs almost exclusively in women.

A typical history given by a patient suffering from the post-menopausal type of osteoporosis is of some vague back pain and then the development of quite severe pain after a minor accident or severe jolt. On examination, rigidity of the spine is found and frequently some scoliosis. Radiographic examination discloses the typical appearances. The shadow cast by the bone of the vertebral bodies is of poor density, although there may be relative sclerosis of the upper and lower borders of the bodies.

One or more crush deformities of the bodies are found, typically in the mid-dorsal and upper lumbar region, and several of the bodies may show the typical fish or hour-glass deformities. These are due to expansion of the elastic intervertebral disks at the expense of the softened vertebræ.

On physical examination these patients tend to show their age prematurely, their skin being noticeably thin, which suggests that the atrophy is more widespread than just in the bone matrix. Anæmia is often present (Cases I and II). I have seen three patients with post-menopausal osteoporosis in whom severe back pain has been precipitated by electroconvulsive therapy. In none of these was the condition suspected beforehand (Case III). Post-menopausal osteoporosis has a predilection for the spine and pelvis, long bones being involved only in the cases of more severe involvement. The skull is notable for its lack of involvement; this is an important point in differentiating the condition from hyperparathyroidism, in which the skull is one of the first bones to show radiological evidence of involvement. Normal serum calcium and phosphatase values also serve to differentiate osteoporosis from hyperparathyroidism. Two other conditions should be borne in mind because of the occasional similarity of the X-ray appearances in the spine—multiple myelomatosis and secondary deposits from breast or lung cancer.

In the first the ribs are involved, with multiple small cystic shadows, and microscopic examination of marrow material obtained by sternal puncture should differentiate the condition. In the latter, evidence of the primary tumour will do so (Case IV).

Although the serum calcium, phosphorus and phosphatase levels are normal, hypercalciuria is frequently found in the initial stages of post-menopausal osteoporosis. A considerable number of these patients, therefore, develop renal stones. This hypercalciuria disappears in the later stages of the disease, when the skeleton is depleted of calcium. Nephrolithiasis is, of course, a common complication of immobilization osteoporosis.

The management of patients with post-menopausal osteoporosis emphasizes some important points. These patients should not be completely immobilized. They should not be treated in recumbency on a plaster bed or frame. If this is done, further porosis occurs as a result of the immobilization. They should be fitted with a support. Care should be taken to see that they have an adequate and balanced diet. Œstrogen or testosterone, or both in combination, should be given, together with calcium and large doses of vitamin *D*. Activity should be encouraged. Testosterone administration is supposed to lead to retention of nitrogen and stimulation of tissue growth by formation of new protein. It is found that these patients lose their pain and feel much better after the administration of testosterone, although there is no radiographic change in their bone condition.

Senile osteoporosis can often be diagnosed even before an X-ray film has been taken. These patients have often lost height, and shortening of the spine with kyphosis and scoliosis is evident on inspection. They look much older than their actual age. The spine is rigid, with points of tenderness along the spinous processes on percussion. With them again, acute symptoms follow a jar or minor trauma. X-ray examination shows the typical hour-glass or fish vertebræ with crush deformities and poor contrast between the porotic vertebræ and the soft tissue shadows (Burrows and Graham, 1945; Burrows, 1950).

Treatment should follow the same lines as for post-menopausal osteoporosis.

Albright (1941) states that osteoporosis may be superimposed on Paget's disease. It is his belief that the sequence of events in Paget's disease is as follows: (*a*) destruction of the bone from unknown cause; (*b*) osteoblastic stimulation due to increased stresses and strains; (*c*) overgrowth of bone and increase in the serum phosphatase level as a result of osteoblastic stimulation. Thus if Paget's disease was superimposed on osteoporosis, one would expect steps (*b*) and (*c*) to be missing because of the primary hypofunction of the osteoblasts.

The possibility of this combination of osteoporosis and Paget's disease should be borne in mind because it probably occurs more commonly than is generally thought. If in any case of Paget's disease in which a fracture is present the X-ray appearances suggest osteoporosis, testosterone, calcium and vitamin *D* should be administered, because further and rapid porosis is apt to occur through the enforced immobilization (Case V). Considerable literature has evolved in recent years on the subject of immobilization osteoporosis.

G. G. Gill (1944) was one of the first to draw attention to the discrepancy in the length of limbs in cases of tuberculosis of the hip in children. He pointed out that arrest of growth followed premature closure of the epiphyseal cartilage about the knee owing to disruption of the epiphysis into the diaphysis with bony bridging of the epiphyseal line. This disruption of the epiphysis is due to the porotic condition of the diaphysis, the result of immobilization.

The condition is further discussed by H. A. Sissons (1952) in the last volume of the British number of *The Journal of Bone and Joint Surgery*. In this number also F. H. Stevenson (1952) discusses the osteoporosis of immobilization in recumbency, showing that prolonged recumbency produces widespread skeletal changes, which in the thorax and both lower limbs are often permanent, and he concludes by stating that while it is not denied that immobilization of a diseased joint may be essential, there is a growing mass of evidence that immobilization in recumbency of the whole patient has severe effects both in the neighbourhood of the actual lesion and upon the skeleton as a whole.

The conclusion to be drawn is important. In the treatment of diseased joints, such as tuberculous hip disease *et cetera*, we should use all measures, including early operation, when possible, to minimize the necessity for prolonged immobilization of the patient as a whole.

Reports of Cases.

CASE I.—Mrs. R. was aged fifty-six years when first examined; she complained of back pain which had become much worse after a lifting strain. When first examined she was having considerable pain both in the lower part of her back and also between her shoulders. She was able to walk only with difficulty owing to the pain in her back; jarring increased the pain. Examination revealed dorsal kyphosis and slight dorso-lumbar scoliosis. No movement of the dorsal or lumbar parts of the spine was possible. The spinous process of the seventh dorsal vertebra was prominent. X-ray examinations revealed hour-glass deformities of many of the vertebral bodies, with crush deformities in several of the mid-dorsal and upper lumbar vertebræ. The bones of the spine were obviously porotic. She was treated with a light full-length spinal support and the administration of œstrogens, testosterone, calcium and large doses of vitamin *D*. She improved generally and lost most of her pain, and now gets about wearing a full-length corset and does her own housework. The X-ray appearances of her spine have not altered over seven years.

CASE II.—Mrs. McD., aged fifty-two years, had sustained a fracture of the shaft of the left femur. It was noted that the bone appeared decalcified in the X-ray film, but union occurred in about fifteen weeks. Five years later she sustained a fracture of the shaft of the right femur; this occurred when she caught her foot in a mat and twisted her leg—she felt the bone snap. It appeared to be a trivial injury. The fracture was treated in the usual way in a Thomas splint, but despite satisfactory apposition of the fragments union had not occurred after five months. The bone texture appeared porotic in the first films, and this porosis became more pronounced as the months passed during which she was immobilized. During an operation for grafting of the ununited fracture the bone was found very soft and friable, as also was bone taken from the iliac crest for the graft. Further investigation revealed generalized osteoporosis affecting most bones, but particularly the spine, pelvis and femora. In the thoracic and lumbar vertebræ pronounced hour-glass deformities were present. The blood chemistry was normal, and examination of marrow from sternal puncture revealed normal findings. Microscopic examination of sections of bone removed by biopsy revealed absorption of bone and replacement by dense fibrous tissue, stated by the pathologist to be osteoporosis of a non-specific nature.

The condition appears to fall into the class of post-menopausal osteoporosis, although the gross changes in the femur are unusual and have probably been induced by the immobolization required during the treatment of the slow union of her fracture.

CASE III.—Mrs. R., aged fifty-seven years, was given electroconvulsive therapy for some form of psychosis. After the first treatment she complained of a painful back. On examination of the patient the lumbar and thoracic spinal movements were found greatly restricted, and tenderness on percussion of the mid-thoracic and thoraco-lumbar regions of the spine was present. X-ray films showed osteoporosis of the thoracic and lumbar bodies with relative density of the upper and lower borders of the bodies. These were crush deformities in the bodies of the seventh and twelfth thoracic vertebræ, with considerable deformity of the seventh. The blood chemistry was normal.

The condition was considered to be one of post-menopausal osteoporosis, unsuspected until the trauma of convulsive therapy resulted in the damage to the spine.

CASE IV.—Mrs. D., aged fifty-five years, was admitted to hospital complaining of pain in the region of the right hip. X-ray examination of the pelvis revealed a fracture of the neck of the right femur with inward protrusion of the acetabulum. The bone of the pelvis and both femora appeared porotic. Further investigation showed this case to be one of multiple myelomatosis. X-ray examination of the spine showed that the bones cast a poor shadow, and the lumbar bodies showed hour-glass deformities; there was a crush deformity of the first lumbar body. The appearances in the X-ray film of the spine are similar to those seen in cases of post-menopausal and senile osteoporosis.

CASE V.—Mrs. T., aged seventy-two years, fell and sustained a pertrochanteric fracture of the right femur. X-ray examination showed changes typical of Paget's disease of this femur and of the innominate bone of the same side. Osteoporosis appeared to be superimposed on this. The femur united under treatment in a Thomas splint. When the patient was commencing to walk the left ulna fractured three inches above the wrist with a trivial strain. Four years later the patient fell and sustained fractures of both femora. On the right side the fracture involved the upper third and on the left side the middle third of the shaft. In the X-ray film of the left femur marked osteoporosis is seen superimposed on Paget's disease. The patient was treated in two Thomas splints. After twelve weeks, when the fractures of both femora had clinically united, her body was twisted to one side by an inexperienced nurse in the course of washing her back (the legs were still slung in the splints). She felt a severe pain in the region of the left hip, and subsequent X-ray examination showed she had sustained a pertrochanteric fracture of the left femur. This remained very painful on any movement; but the pain disappeared quickly, and union occurred after the daily administration of testosterone with vitamin *D* and calcium.

Summary.

1. The pathology of osteoporosis is briefly discussed, with an enumeration of the common clinical types met with in practice.

2. The symptoms, signs and radiological findings in post-menopausal and senile osteoporosis are described, together with some points in the management of these cases.

3. The association of Paget's disease and osteoporosis is discussed.

4. A brief mention is made of osteoporosis associated with immobilization, and of the conclusions to be drawn.

5. Some illustrative cases are reported.

References.

ALBRIGHT, F., SMITH, P. H., and RICHARDSON, A. M. (1941), "Postmenopausal Osteoporosis: Its Clinical Features", *J.A.M.A.*, 116: 2465.

BURROWS, H. J., and GRAHAM, G. (1945), "Spinal Osteoporosis of Unknown Origin", *Quart. J. Med.*, New Series, 55: 147.

BURROWS, H. J. (1950), "The Bone Dystrophies", in "Modern Trends in Orthopædics", edited by Platt, H., London, Butterworth: 400.

GILL, G. G. (1944), "The Cause of Discrepancy in Length of the Limbs following Tuberculosis of the Hip in Children", *J. Bone & Joint Surg.*, 26: 272.

"GOULD'S MEDICAL DICTIONARY" (1941), 5th Edition, Blakiston, Philadelphia.

SISSONS, H. A. (1952), "Osteoporosis and Epiphyseal Arrest in Joint Tuberculosis. An Account of the Histological Changes in Involved Tissues", *J. Bone & Joint Surg.*, 34B: 275.

SNAPPER, I. (1949), "Medical Clinics on Bone Disease", 2nd Edition, Interscience Publishers (New York and London).

STEVENSON, F. H. (1952), "The Osteoporosis of Immobilisation in Recumbency", *J. Bone & Joint Surg.*, 34B: 256.

BONE INFECTION: ITS PROBLEMS AND ATTACKS, WITH SPECIAL MENTION OF STREPTOKINASE AND STREPTODORNASE.[1]

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EVERY orthopædic surgeon has experienced dismay when his bone graft becomes infected. There have been many elaborations of technique aimed at eliminating this mishap, but it still occurs. This paper discusses methods of control and elimination after the event, be it from surgical interference, from trauma or from spontaneous hæmatogenous sources.

Severe bone infection is common after war wounds, and the history of its control shows that each major advance has occurred during shooting wars. Surgical *débridement* and Carrel-Dakin irrigation saved many lives during the 1914-1918 war, whilst Trueta showed the efficiency of the Winnett-Orr technique in Spain. Finally, during World War II, Florey at Oxford developed penicillin, already discovered by Fleming, and wartime conditions led to its production and large-scale clinical trial with early proof of its remarkable powers.

[1] Read at the annual meeting of the Australian Orthopædic Association, Hobart, September 9 to 12, 1953.

Clinical Pathology.

The *Staphylococcus aureus* causes 90% of bone infections. This organism has become more prevalent and a greater nuisance these last few years, particularly in our bigger hospitals, where very often the majority of strains are found to be penicillin-resistant. Most of the remaining 10% of infections are caused by the streptococcus or pneumococcus, more particularly in children; and we must remember the odd infection due to varied organisms such as *Bacillus typhosus*, Brucella and others (Sherman, 1949).

Acute Osteomyelitis.

Acute osteomyelitis is a small problem as a rule, but early adequate and correct antibiotic treatment is necessary to prevent it becoming chronic. Proper and early drainage of pus prevents extension and pain; and if the wound is closed primarily convalescence is rapid.

Chronic Bone Infection.

Chronic bone infection may be hæmatogenous or may follow contamination of traumatic or surgical wounds. Antibiotics have reduced the frequency of the almost malignant recurring chronic hæmatogenous osteomyelitis, although it still presents a difficult problem. Often there is widespread and deep involvement of the pelvis or of multiple sites, so that it is impossible to perform complete surgical removal of infected bone and sinuses.

Infection which follows compound fractures of the extremities in old people with inadequate peripheral circulation is another difficulty. Stasis and œdema from prolonged recumbency allow the organisms to be walled off by fibrous tissue in pockets inaccessible to antibiotics given parenterally. Secondary contamination by Gram-negative organisms produces foul discharge and prevents bony union of fractures and excoriates the skin. The skin is inelastic, the swinging of even double-pedicled flaps is risky, and sloughing is apt to occur when closure is attempted.

The Problem and a Lead.

What is the best way to handle this problem? How can we best utilize the antibiotics which, though expensive, are freely provided by the present Commonwealth Government? Can we eliminate these distressing cases? Or are we going to contaminate the nurses' throats with resistant organisms which will plague our operations of election in our hospitals?

The key is revealed in an article by Florey and Florey (1943), who after a critical review of the potentialities of penicillin, then not generally available in Britain, discuss the results of the treatment of mastoid infection by what they describe as "suitable surgery". A number of patients with chronic mastoid infections were operated on by a modified Swartz procedure. The infected bone cells were removed by the usual saucerization but the skin was sutured carefully together. A small catheter was included in the wound and its mouth closed by a spigot. A solution containing 500 units per cubic centimetre of penicillin was run in every six hours, preceded by aspiration on each occasion. Penicillin was administered parenterally at the same time. After seven days the catheter was removed. Almost all the wounds healed by first intention.

Florey *et alii* (1947) again showed that Gram-negative organisms are not innocuous contaminants. They investigated bacteriologically the progress of 63 lacerated wounds. Their initial object was to compare the progress of healing of wounds infected by Gram-negative and Gram-positive organisms. However, it was discovered that in almost all cases the Gram-positive organisms were eliminated by penicillin given parenterally or parenterally and topically. In almost all cases the wounds were contaminated by Gram-negative organisms two weeks after their infliction. In one case the wound was contaminated by a different Gram-negative organism after each major dressing. In most cases these organisms did not do very great harm; but once well established they produced a characteristic bone swelling, discharge, delayed bony union, and chronic sinuses which were disconcerting, because these sinuses were sealed off temporarily by the growth of epithelium, which was not stopped by these contaminants. Five wounds which were not secondarily infected by Gram-negative organisms healed rapidly, and union occurred at the same rate as for a corresponding closed fracture.

Principles of Treatment.

These principles were used in the treatment of a number of patients. Early adequate and correct antibiotic parenteral therapy was combined with "suitable surgery". The infected area was completely excised, and the wound was closed without drainage. It is considered important to prevent the loss of the hæmatoma which fills the wound cavity, as it forms a scaffold for early repair and contains a high concentration of the topically applied antibiotic.

In cases in which the hæmatoma was lost, healing occurred by slow granulation, with almost inevitable contamination by Gram-negative organisms. If this occurred, control was attempted by using small catheters and filling the wound locally with antibiotic solutions. If surgery had been inadequate chemical curettage was used in combination.

Buchman and Blair (1951) applied Florey's principles, beginning with the parenteral administration of penicillin alone. They then combined this with surgical drainage and topical application; they found healing by granulation was slow and ineffectual. The most noticeable improvement in their results occurred when they closed the wounds by delayed primary suture, waiting until they thought that the infective process was under control. Their next logical step was to close the wound immediately after operation. Their results were still better.

Prigge (1946) elaborated the surgical excision of the infected material by swinging vital muscle flaps into the resulting cavity. Coleman *et alii* (1946) used cancellous bone chips to the same end. Buchman, in the discussion following his paper, makes it clear that the hæmatoma is a surer method of reconstituting the damage of excision. He points out that bone chips, even if cancellous, cannot be kept aseptic even if bathed in strong antibiotic solutions, and that muscle flaps frequently degenerate into masses of hard fibrous tissue. We know that the hæmatoma organizes to form the callus about the ends of fractures, and provided that there is local control of organisms and dangerous sources of them have been removed by adequate surgery it will act in a similar manner in these cases.

The Method.

A full review of the patient's history includes a note of previous operative procedures, previous antibiotic treatment and any allergic reactions. In the physical examination the availability of a good post-operative skin cover must be considered. Skiagrams, including those taken after lipiodol injection into tracts, are necessary to localize sinus tracts and sequestra, and to plan the surgical measures.

On the patient's admission to hospital, cultures are made to determine the organisms present and their sensitivity to all antibiotics available. General measures are instituted to combat anæmia, hypoproteinæmia or avitaminosis. The administration of penicillin, 100,000 units per cubic centimetre, or proper doses of the chosen antibiotic is begun twenty-four hours before surgical treatment.

Surgical excision must be as complete as is possible. Sinus tracts are excised, together with as much surrounding fibrous tissue as possible, the bone is saucerized, edges are levelled and the cavity is extended beyond the lesion into normally vascularized bone. All bone sand and débris are washed out with normal saline, and the cavity is filled with pure powder of the appropriate antibiotic. The wound is carefully closed in layers, and the skin is approximated with interrupted sutures. The limb is supported by a compression bandage. Plaster splints are used only if there is danger of pathological fracture.

After operation the wound is left undisturbed unless there is a severe general reaction. Stitches are removed in ten days. The patient is encouraged to get up in a few days if it is an upper limb. When a lower limb is involved he is kept in bed for three to four weeks after operation.

The Surgically Inaccessible Case.

Sometimes it is impossible to remove all sources of chronic infection because of the anatomy or function of the involved area. After loss of the hæmatoma, because of poor skin cover or activity of infection local therapy is instituted. Penicillin solution (20,000 to 50,000 units per cubic centimetre in normal saline) or streptomycin solution (125 to 250 milligrammes per cubic centimetre) is run into the wound through small catheters. These are not drainage tubes and should be sealed off. Sufficient solution is used to fill the cavity. This is repeated at six-hourly intervals. If this is to be successful, seven to ten days' treatment is enough.

Complementary to this attack is the use of "physiological curettage". Streptokinase, an enzyme prepared from certain strains of the streptococcus, produces fibrinolysis when it combines with serum euglobin and will liquefy old clot. However, it will not attack fibrous tissue. Streptodornase, an enzyme group, is prepared similarly, but is directly proteolytic in action, digesting sloughs. Streptokinase (100,000 units) and streptodornase (25,000 units) are supplied in ampoules as "Varidase", and, dissolved in five to twenty cubic centimetres of normal saline combined with antibiotic if necessary, are introduced into the wound through catheters. When these enzymes are used the tubes are not clamped and the outpouring of tissue fluids which results is drained away. These enzymes have no effect on living cells. There may be a feverish reaction and allergic reactions have been reported; otherwise there seem to be no acute or delayed toxic effects.

Reports of Cases.

CASE I.—A., a male patient, aged fifty-three years, a very heavily built man with poor peripheral circulation, sustained an oblique closed fracture of the lower third of the right tibia, on January 18, 1949.

Union did not occur, and a sliding bone graft was inserted on May 15, 1950, seventeen months later. Four months later, in September, 1950, he resumed work on the wharves. On December 14, 1951, an ulcer appeared, and finally he developed a frank bone infection with a discharging sinus. The screws were removed from the graft in May, 1951.

The patient first came under my care in July, 1952. His left leg was swollen and the skin was discoloured and dead looking; bone was visible through a gaping slit one inch long. The œdema was controlled by elevation and the application of a compression bandage. The organism was identified as *Staphylococcus aureus*, which was sensitive to all antibiotics except penicillin. He was given streptomycin parenterally. At operation the bone graft was well incorporated, but could be identified easily because it was avascular. Several pockets between the fracture ends were cleaned out, but the graft was left intact. The wound was closed over penicillin and sulphanilamide powder. The sinus persisted, and there was a small but constant discharge.

The patient was admitted to hospital on three occasions, and local reaction was controlled by the topical application of penicillin and streptokinase and streptodornase, but the sinus still persisted.

On July 28, 1953, the pathologist reported that the organisms which were now well mixed were sensitive. This was considered doubtful. Under a combined penicillin and streptomycin cover, what was left at the sliding graft was completely removed, a long gutter being left. The wound was closed by primary suture. Healing is still slow and a cross-leg flap will be necessary to obtain skin closure.

CASE II.—B. was crushed by a boom on November 8, 1949. He had a comminuted open fracture of the upper third of the right tibia and fibula. The wound was debrided, the tibia was plated and the skin was closed.

On examination of the patient on September 20, 1950, X-ray examination revealed very frail union, and the fragments held by a six-hole plate. There was a deep gutter where the wound had been, and a small sinus opened into the floor of the wound.

At operation on January 10, 1951, the plate and debris were removed, and the wound was filled with penicillin and sulphanilamide powder. Healing was not complete after ten days, and streptomycin was given locally by tubes for seven days, with final complete healing. After twelve months the frail union had consolidated, and the patient was taking full weight and was back at work.

CASE III.—C., a hairdresser, aged forty-three years, reported to the casualty department in October, 1950, with a cut left index finger. He was given antitetanic serum into the left humerus. He developed lymphangitis and an abscess at the site of the injection. When first examined in December, 1950, the patient had two granulating sinuses over the lateral aspect of the left humerus below the deltoid insertion. There was radiological evidence of local bone involvement. Streptococci, β-hæmolytic and sensitive to penicillin, were grown in culture from the sinus.

At operation on February 2, 1951, excision and partial closure were attempted under penicillin "cover". This operation was incomplete, and drainage persisted. A second operation was performed in March, 1951; complete and careful removal of all infected material was carried out under chloramphenicol "cover". However, the hæmatoma discharged and the skin edges collapsed leaving a small sinus. This healed; but in May, 1952, he slipped and sustained a compound fracture at the site involved. The opening was small, and he was treated in a spica until July, 1952.

In August the bone had healed, and there was no radiological evidence of the infective process. A small area of bone was visible in the floor of the now funnel-shaped wound.

In September, 1952, the skin edges were freed and the flaps resutured; healing occurred in six weeks.

CASE IV.—D., aged forty-five years, a male postal employee, was admitted to hospital on October 21, 1952, complaining of stiffness and irritability of the right elbow of eight months' duration. He had no previous personal or family history of tuberculosis.

On examination of the patient, his right elbow was swollen, red and hot, the muscles of the arm and forearm were wasted, and movement was limited to 15° of extension (90° to 105°) and flexion from 90° to 60°. X-ray examination revealed general decalcification of the bones about the elbow joint. There were areas of moth-eaten rarefaction about the head of the radius and the lateral epicondyle.

Operation was undertaken on October 24. The elbow joint was exposed by a posterior approach, pus and caseous matter were evacuated, and the articular surfaces were excised to free normal appearing bone. One gramme of streptomycin was instilled and the wound was closed. The elbow was immobilized in a padded plaster cast, and an abduction frame was fitted next day. Streptomycin was given in doses of 0·5 gramme twice a day, and PAS, 12 grammes per day in four doses. This was continued for three months.

On November 14 the plaster cast was changed; the wound had healed. A further plaster cast was applied.

In February, 1953, the plaster cast was removed; the arm was fixed at an angle of 100°, and there was no local reaction or general disturbance. A moulded leather cuff was prepared. The patient resumed his occupation as a postal employee after one more month.

The pathologist reported the presence of acid-fast bacilli and areas characteristic of tuberculous disease.

CASE V.—E., aged seventeen years, a labourer, was admitted to hospital on June 30, 1952. He had developed osteomyelitis at the age of seven years when in Germany; this involved the upper part of the right tibia and the lower part of the left tibia. The treatment was by drainage—on the right side at that time and on the left side three years later. The left ankle had become swollen and painful three months before his admission to hospital.

On examination of the patient his left ankle was red and swollen; tenderness was present across the front of the ankle, and ankle movement was restricted by pain. Moderately severe intermittent pyrexia was present.

On July 13, 1952, the operation of saucerization was performed and penicillin powder was used. Immediate closure was employed, but a large drainage tube was stitched into the cavity in the lower end of the wound. Post-operatively there was complete evacuation of the hæmatoma, giving the impression of serious hæmorrhage. Penicillin and saline topical application was given through the tube. About an inch of the lateral flap sloughed and separated, but no organisms were demonstrated in the discharge. This led to a longer period in hospital, and the patient was discharged on September 1, nine weeks after his admission, with the wound almost healed. The organism in this case was the *Staphylococcus aureus*, coagulase-positive. It was sensitive to all antibiotics except streptomycin.

CASE VI.—F., a male patient, aged twenty-six years, presented with a history of recurrent painful swelling of the left ankle present for the last ten years. He had had an operation on this same left ankle sixteen years earlier in the country, and an operation had been performed by what was

apparently the Winnett-Orr technique. The patient said that the wound had taken a number of weeks to heal and had been dressed with "Vaseline" packs.

Examination of his left ankle revealed an old surgical scar six inches long running vertically down the front of the lower third of his left tibia. There were no sinuses and the skin was in good condition. There was a rounded thickening of the lower end of the tibia, which was hot but not red. Tenderness was present above the medial malleolus. The X-ray examination revealed two cystic areas, one at the junction of the middle and lower thirds and another in the lower end.

Operation on April 24, 1953, with the use of a tourniquet, consisted of saucerizing the lower third of the tibia. The lower cavity contained creamy yellow pus and was walled by dense sclerotic bone. The sclerotic walls were chiselled away, and the cavity was filled with penicillin and sulphanilamide powder and closed by interrupted sutures. There was some sloughing along the skin edges, but the wound was completely healed in four weeks.

CASE VII.—G., a female patient, aged thirteen years, on January 29, 1953, ran a needle into her hand. A pulp space infection was drained by splitting of the web.

On February 24, 1953, she presented with a fusiform swelling of the proximal phalanx of her left ring finger. X-ray examination revealed an eroded proximal phalanx.

Operation consisted of lateral exposure of the proximal phalanx and simple drilling of the bone; no definite sequestra were visible. A tube was stitched into the wound, and penicillin and "Varidase" in normal saline were instilled every six hours and once a day respectively. The tube also acted as a drain.

On May 14 a sequestrum measuring one centimetre by 0·5 centimetre was removed. The wound healed finally with some shortening of the phalanx and limitation of flexion and extension of the finger.

Summary.

Some of the problems of bone infection are discussed. The controlled use of antibiotics combined with "suitable surgery" is advocated in the treatment of chronic osteomyelitis; this consists of radical excision of the infected area and primary skin closure under parenteral antibiotic cover. The local use of antibiotics and the retention of the hæmatoma are considered the best way of obtaining early healing and reconstitution of bone defects and of avoiding secondary contamination by Gram-negative organisms.

Physiological curettage and the topical application of antibiotics are considered for the treatment of extensive chronic infection which cannot be handled by radical surgery because of inaccessibility or the presence of resistant organisms.

References.

BICKEL, W. H., and BATEMAN, J. G. (1949), "Treatment of Chronic Hematogenous Osteomyelitis by Means of Saucerization and Bone Grafting", *Collect. Papers Mayo Clin.*, 41: 415.

BUCHMAN, J., and BLAIR, J. E. (1951), "The Surgical Management of Chronic Osteomyelitis by Saucerization, Primary Closure and Antibiotic Control; Preliminary Report on Use of Aureomycin", *J. Bone & Joint Surg.*, 33-A: 107.

CARRELL, B., and WOODWARD, J. W. (1950), "Chronic Osteomyelitis: Primary Closure following Saucerization; Preliminary Report", *J. Bone & Joint Surg.*, 32-A: 928.

CALDWELL, G. A. (1945), "Secondary Infection of Wounds", *Ann. Surg.*, 122: 641.

COLEMAN, H. M., BATEMAN, J. E., DALE, G. M., and STARR, D. E. (1946), "Cancellous Bone Grafts for Infected Bone Defects; Single Stage Procedure", *Surg., Gynec. & Obst.*, 83: 392.

FLOREY, M. E., and FLOREY, H. W. (1943), "General and Local Administration of Penicillin", *Lancet*, 1: 387.

FLOREY, M. E., ROSS, R. W. N. L., and TURTON, E. C. (1947), "Infection of Wounds with Gram-negative Organisms; Clinical Manifestations and Treatment", *Lancet*, 1: 855.

GRAHAM, F. M., COVENTRY, M. B., and GHORMLEY, R. (1948), "Penicillin in the Treatment of Chronic Osteomyelitis", *Proc. Staff Meet., Mayo Clin.*, 22: 589.

HOWARD, L. G., and others (1950), "Treatment of Chronic Osteomyelitis with Penicillin and Primary Closure of Operative Wounds", *Arch. Surg.*, 60: 112.

LEGGE, R. F., and SCHWINGEL, W. H. (1950), "Evaluation of the Treatment of Chronic Osteomyelitis", *U.S. Armed Forces M. J.*, 1: 514.

METCALFE, J. W. (1949), "Bacteriostatic Coagulants as Fillers in Bone Surgery", *U.S. Navy M. Bull.*, 49: 1067.

PRIGGE, E. K. (1946), "Treatment of Chronic Osteomyelitis by Use of Muscle Transplant or Iliac Graft", *J. Bone & Joint Surg.*, 28: 576.

SHERMAN, M. S. (1949), "Acute and Chronic Osteomyelitis", *Surg. Clin. North America*, February: 117.

SMITH, W. S., and GANEY, J. B. (1950), "Streptomycin in Chronic Traumatic Osteomyelitis", *Arch. Surg.*, 60: 125.

VENABLE, C. S., and PULASKI, E. J. (1950), "Planned Timing in Treatment of Chronic Osteomyelitis under Antibiotic Control", *Am. J. Surg.*, 80: 649.

CHANGE IN THE HIP JOINT IN CEREBRAL PALSY.[1]

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X-RAY examination and a few clinical observations were made on the hip joints of 49 children attending the Ashford Spastic School. Their ages ranged from five to sixteen years. The following classification, not absolute but sufficiently clear, has been based on radiographic appearances:

1. Normal ..... 10 patients
2. Increase in size of lesser trochanter only .. 14 patients
3. Flattened roof of acetabulum ..... 3 patients
4. Elevation of distal component of Shenton's line without subluxation ..... 16 patients
5. Subluxation of one or both of the femoral heads ..... 6 patients

Enlargement of the lesser trochanter is one of the most characteristic features. Examinations were made with the subject's thighs in neutral position, the toes pointing vertically. Of the separate hip joints, the lesser trochanter was normal in 28, slightly enlarged in 43, considerably enlarged in 23, and greatly enlarged in four. The greater increases were present in groups 3, 4 and 5 only.

The appearance of flattened roof to the acetabulum is also seen in some of the group 4 cases. It may be an alternative to subluxation when stress is applied to the joint; but in one case of peculiar cerebral damage both this and considerable enlargement of the lesser trochanter are present despite almost complete atonia of the legs.

Interruption of Shenton's line without subluxation is apparently due to upward displacement of the acetabulum. The resistance to subluxation has been sufficient to arrest the displacement and build a restraining rim. In some of the younger children the buttress has not developed; there is minimal subluxation—less than one-eighth of the femoral head—and it is not clear whether in these cases subluxation will occur later.

Subluxation is present in seven hips in six cases. There does not seem to be much upward displacement. The acetabulum is correspondingly shallow. The head may become deformed or displaced laterally from the top of a very valgoid neck. Appearances similar to those in *osteochondritis juvenilis* were not observed.

Angle of Neck to Shaft of Femur.

The angle of neck to shaft of femur varies inversely with the angle of active leg abduction and angle of stretch leg abduction (Table I).

TABLE I.

Group.	Average Angle of Neck.	Average Free Abduction.	Average Stretch Abduction.
1	143°	62°	76°
2	148°	56°	73°
3	160°	63°	89°
4	156°	39°	68°
5	162°	18°	55°

[1] Read at the annual meeting of the Australian Orthopædic Association, Hobart, September 9 to 12, 1953.

Group 3 comprises only three patients, one of whom had atonia of the leg muscles, and another has had adductor tenotomies.

Shenton's line was interrupted in 27 hips (without subluxation), the average angle of the neck being 157° and varying from 143° to 170°.

Subluxation did not occur with a neck angle of less than 160°, but averaged 166°.

Residual Hip Flexion.

In groups 1, 2 and 3 residual hip flexion is absent or is of only a few degrees. In groups 4 and 5 it is absent in only four cases and may be present to as much as 45° to 50°. It is vaguely in relation to the anatomical variations in the trochanter and acetabulum.

Locomotion.

All patients with one exception in groups 1 and 2 have free locomotion. In groups 3, 4 and 5, eight have free movement, six require walking apparatus, and 12 can only sit. The addition of simple assistance, such as a short iron and T strap, is not regarded as making them dependent on gear.

Intelligence.

Though the average intelligence deteriorates a little in the more severely affected groups, there is no strict relationship, good intelligence and extreme retardation being present in all groups.

Tenotomy.

Division of the *adductor longus* and of the anterior branch of the obturator nerve was performed in only three cases, the aim being to make the wearing of apparatus more practicable. Hip joint changes were already established.

Conclusions.

1. The ilio-psoas action must play a considerable part in causing the changes in the architecture of the hip joint.

2. Upright locomotion with weight bearing may be of aid in forming a substantial rim to the acetabulum and preventing subluxation.

SCOLIOSIS.[1]

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THE problem of scoliosis remains a formidable one in spite of major advances made in this field in the past two decades. If, however, we accept the fact that the results which may be obtained from the treatment of this condition, compared with the normal spine, are poor, from the patient's point of view, even small corrections are major achievements.

The method of measurement of the scoliotic curve introduced by Ferguson in 1930 and later modified by Cobb in 1948 was a major advance, which led to accurate assessment of a curve and the ability to follow it through its evolution and evaluate its treatment.

This method, which is now well known, consists of determining the extent of a curve by the change in the depth of the intervertebral disk spaces. At the limits of the curve the disk space is equal in depth throughout its width. Alternatively, a single vertebra may take part in the formation of two curves, then the disk spaces above and below it are open on opposite sides. This is then described as a neutral vertebra. A perpendicular is drawn from the plane of the vertebra at each end of the curve and the angle is measured where they intercept.

[1] Read at the annual meeting of the Australian Orthopædic Association, Hobart, September 9 to 12, 1953.

Ponseti and Friedman in 1950 were the next to make their valuable contribution in a paper on "Prognosis in Idiopathic Scoliosis". Although the curve patterns they recognized had first been described by Schulthess in 1905, their important contribution related to the deformity that could be expected from each curve pattern.

It is to this prognostic aspect that the major part of the present paper is devoted.

It is first necessary to distinguish a postural from a structural curve. This is readily done by watching the patient as he bends forward and observing any rotation associated with the curve. This is obvious from a rib hump in the thoracic region or a prominence of the *erector spinæ* of one side in the lumbar region. If rotation is clinically absent, the curve is a postural one. This feature applies also to the so-called secondary curves in a true structural scoliosis. These curves are essentially postural, in that they are compensatory to the primary curve and do not show rotation.

This method is often the only means of distinguishing a quadruple pattern from a triple pattern, since radiological evidence is often misleading.

The Factors in Prognosis.

The factors in prognosis are: (i) age of onset, (ii) curve pattern, (iii) ætiology.

Age of Onset.

Irrespective of the ætiology, the age of onset of a scoliosis frequently determines the severity of the final result. It is obvious that structural changes occurring in the spine are magnified according to the amount of spinal growth remaining.

The groups described by James, related to idiopathic scoliosis in particular, are as follows: (i) Infantile. The scoliosis in this group is usually thoracic and in boys. The curve is nearly always to the left. The prognosis is 100% bad. (ii) Juvenile. The scoliosis is usually thoracic, but sometimes thoraco-lumbar. The prognosis is 85% bad. (iii) Adolescent. The scoliosis may assume any pattern, but includes the lumbar curve, which never occurs before the age of ten years. In this group the scoliosis is usually in females and the curve is as a rule to the right. The prognosis is 55% bad. These figures, of course, apply only to idiopathic scoliosis.

In the adolescent patient it is necessary to determine how much spinal growth remains, since the cessation of spinal growth brings with it the cessation of the increase of curvature. This period is fortunately marked by Risser's sign, which is the radiological determination of the extension of the iliac apophysis from the anterior to the posterior superior iliac spine. Alternatively, in females, this period is generally about one year after the onset of menstruation.

If either of these signs is apparent when the curve is still minimal, it can confidently be expected that little increase will occur.

It is, however, during the adolescent period that most of the spinal growth occurs, and in consequence most of the increase in deformity. This factor is obvious by the rapid increase in sitting height that occurs during that period.

The Curve Pattern.

Although the curve pattern mainly applies to prognosis in idiopathic scoliosis, it just as well applies in other types if other factors are equal.

The curve patterns described by Ponseti and Friedman in their series of 444 cases of idiopathic scoliosis are as follows: cervico-thoracic, 1·3%; thoracic, 22·1%; thoraco-lumbar, 15·9%; combined thoracic and lumbar, 37·1%; lumbar, 23·6%. There is an impression that in other series the thoracic pattern is much commoner than in this series.

The cervico-thoracic pattern is fortunately a rare pattern, but results in a very ugly deformity with an appearance of the head rising from one side of the trunk.

The thoracic pattern is an important and common pattern, since severe curves in this region lead to gross rib rotation. The curves are often severe, sometimes measuring 150°. Very little compensation above the primary curve is possible without alteration of the line of the neck, and a severe list is consequently present. The shoulders are unequal in height and a hip is uncovered. However, the major part of the deformity is the severe rib hump.

In the thoraco-lumbar pattern the apex of the curve is usually at the eleventh or twelfth cervical vertebra, and it is intermediate in type between the thoracic and the lumbar patterns. There is a sufficient length of the thoracic part of the spine above the curve to allow compensation without the production of a severe list. In addition, a gross rib hump is not present.

The combined thoracic and lumbar pattern is the only quadruple pattern and has an earlier onset than the average. Both the thoracic and lumbar curves are primary, and in spite of gross radiological appearances the clinical deformity is minimal. The shoulders are level, the hips are covered, and because the posterior rotations balance there is no apparent kyphosis.

In the lumbar pattern the apex of the curve is at the first, second or third lumbar vertebra. This is one of the least deforming patterns, and depends on the following factors: (i) The curve is late in onset. It is not known for an idiopathic lumbar curve to begin before the age of ten years. (ii) It rarely progresses to a severe extent. (iii) There is no rib rotation associated with it. (iv) There is a large length of spine above to compensate.

Ætiology.

It is intended to discuss ætiology only in so far as it influences prognosis.

The Paralytic Curve.—Variations in the paralytic type of curve are legion, but there are two outstanding groups: (i) the true paralytic curve due to muscle imbalance; (ii) the collapsing curve, in which there is a severe symmetrical paralysis. The characters of the former type are that the curves are long and are easy to correct. The main factor in their causation is unilateral weakness of the intercostals or the lateral abdominal muscles. The *erector spinæ* muscles play a small part, but a corresponding segment is usually involved with the other muscles. Muscle imbalance is a greater factor than the severity of the paralysis.

The Neurogenic Type.—Neurofibromatosis in particular causes a characteristic curve. This is often of early onset and is severe. It is usually a short thoracic curve and is associated with other manifestations of neurofibromatosis. It always progresses and has a very bad prognosis.

The Congenital Type.—Frequently severe radiological anomalies are associated with only mild clinical deformities. This curve pattern is evident at birth and does not tend to progress. It is possible to have congenital anomalies causing curves which cancel themselves out. However, it was not uncommon in James's series to find an idiopathic pattern associated with a congenital curve at another level. This may serve as a pointer to the ætiology of the idiopathic type. It is interesting to note that congenital scoliosis due to a lumbo-sacral anomaly is the only cause of a double curve apart from a short leg.

Comment.

The importance of prognosis in scoliosis, then, is in sparing from treatment patients who will not develop a severe deformity. In a report of the Research Committee of the American Orthopædic Association in 1941, 92% of their patients presented for cosmetic reasons only, the remainder because of backache.

Treatment.

It is important to emphasize the fact that the use of exercises and jackets in the prevention of progression of scoliosis is finding less and less favour. The report of the American Research Committee into this problem found the following results with exercises alone: the condition of 35% of patients remained unchanged, the scoliosis of 34% increased by 5° to 15°, that of 27% increased 20° and over, and the condition of 5% improved. The improvement in this last-mentioned group was so minimal as to be due to errors of mensuration.

It was found that the effect of corrective jackets was completely lost when the jacket was abandoned, unless its use was combined with spinal fusion.

The management of scoliosis, then, resolves itself into the following measures: (i) no treatment for those patients who are unlikely to develop a severe deformity; (ii) correction by a turnbuckle jacket and spinal fusion for those in whom the curve will be severe.

It is necessary now to decide what constitutes a severe curve. This will vary according to the position in the spine which the curve occupies; but generally a curve of 70° and over produces enough clinical deformity to be classed as severe.

If it is borne in mind that most curves are first noticed in early adolescence, it is not surprising to find that only 5% come into the category of severe deformity. The curves warranting correction, then, are the following: (i) those over 70° producing severe clinical deformity; (ii) those of an early onset and poor prognostic position, which are likely to progress to a severe deformity; (iii) the collapsing paralytic spine; (iv) very rarely, the severe lumbar curve which produces uncontrollable backache.

If correction and fusion are decided upon, it is first necessary to determine the mobility of the secondary curves. This is possible by the use of the method of the bending film introduced by Cobb. This procedure consists of bending the patient in the lateral plane in the direction of the primary curve. This eliminates the secondary curves except for their residual rigidity. The sum of the rigidity of these curves is, then, the amount to which the primary curve may be corrected. Should correction go beyond this point, the patient will be left with a list to one side. A list may not always occur, since relapse to a greater or lesser extent often follows spinal fusion; but this cannot be relied upon to occur when necessary.

The Risser jacket holds the greatest promise as a means of correcting the primary curve and is well enough known to warrant no further description.

The type of spinal fusion is a matter of individual choice, but some American figures show that pseudarthroses developed as follows: in the Hibb's type of fusion, in 29% of cases; in the Hibb's type *plus* bone graft, in 33%; in the Albee type, in 25%; in the McKenzie-Forbes type, in 23%; in the Klienberg strut type, in the one case reported. James, in 50 cases in which a chip graft of homogenous bone was used, reports the occurrence of only two pseudarthroses.

It is sometimes necessary, when a long curve is to be fused, to do this in segments at separate operations, or alternatively to fuse one side of the curve at a time. The amount of spine to be fused is the primary curve alone. Extension into the secondary curves does not lead to increased stability, but decreases the compensation that may occur in these curves.

The spinal fusion is best carried out through a trap-door opening in the Risser jacket, in which the patient remains until fusion is complete. This period is generally about six months. It is as a rule considered necessary that the graft should be protected by a spinal jacket for a further six months.

The collapsing paralytic spine is worth a special mention, in that fusion down to the sacrum is usually necessary. Before this is done it is imperative to determine whether the patient has adequate hip flexors. If these are deficient, it is impossible for the patient to walk, since tilting of the pelvis is eliminated by fusion of the spine to the sacrum. In doubtful cases a plaster jacket should be applied to eliminate lumbo-sacral movement, and then the patient should see if he is able to walk.

The only remaining factor is the age at which fusion should be carried out.

It is apparent that the earlier correction and fusion occur, the easier is the correction of the primary curve and the less rigid are the secondary curves; also the deformity will not have advanced to its full extent. Against this is the possibility of a lordotic deformity which has previously followed early fusion, and the difficulty in obtaining sound bony ankylosis. James has not up to date carried out fusion before the age of ten years. Other workers have fused congenital curves in patients as young as eighteen months, but unfortunately their results are not to hand. From this treatment correction of the lateral curve will result to a greater or lesser degree. The rotation and its associated deformities unfortunately remain.

In conclusion, correction and fusion offer excellent results in well-chosen cases; these are the unfortunate 5%. In the remainder no treatment is justified at all.

RECURRENT DISLOCATION OF THE PATELLA.[1]

By FRANKLYN STONHAM,
Melbourne.

THE patella may become dislocated repeatedly from a variety of causes, as follows.

Developmental Anomalies.

The patella may develop in an abnormal position in the quadriceps tendon and out of its correct alignment, and thus tend to be pulled away from its proper position between the femoral condyles, usually laterally. This condition may be familial and hereditary. Often the patella in such cases is abnormally small and the condition may be bilateral, or on one side the patella may be absent or bipartite. The edge of one or other of the femoral condyles, usually the outer, may be absent or imperfectly developed so that an inclined plane prises the patella from its proper alignment.

Dislocation Associated with Genu Valgum.

When *genu valgum* is present, the quadriceps tends to pull the patella over to the lateral aspect of the joint, and it is usually associated with poor muscular development and general ligamentous laxity.

Dislocation Following Traumatic Dislocation.

When dislocation follows traumatic dislocation, it is due to contraction and scarring of the lateral part of the capsule of the knee joint and the lateral part of the quadriceps expansion. The corresponding structures on the medial side of the joint are stretched and attentuated or actually deficient. The patella does not slip off the femoral condyles; it is actually pulled off by strong tissues binding the patella to the lateral aspect of the proximal extremities of the tibia and fibula, and flexion is possible only if the patella passes laterally and allows the lower end of the femur to bulge the medial slack portion of the quadriceps expansion.

Clinical Features.

The patient may complain of the knee suddenly giving way, this being followed by inability voluntarily to straighten it. Pain and effusion follow. In other cases the patella may slip laterally while the knee is flexed when the patient is sitting. Most patients are aware that the patella becomes dislocated and can demonstrate the abnormality. The joint appears widened and the patella can easily be seen and felt in its abnormal situation. In a child the history of giving way with inability to straighten, followed by effusion, may suggest a torn meniscus; but injuries to the menisci are not common in children, and adults who suffer from this disability can as a rule give a more suggestive description of their symptoms together with an account of previous trauma. Partial subluxation may cause attacks of pain only, and recognition of the condition may be more difficult.

Treatment.

If the dislocation is associated with knock-knees, the knock-knees should be treated by splints or osteotomy according to the degree of deformity and the age of the patient. Subsequent physiotherapy directed to improving the power of the quadriceps may and usually does cure the condition. In many cases in which the condition is due to congenital abnormalities, physiotherapy may effect a cure. If such conservative measures fail, operative treatment would be indicated, and in most traumatic cases operative measures are required.

Operations.

A variety of operations have been devised to treat the condition.

1. The patellar tendon may be detached with a block of bone from its insertion and reinserted in a more medial position. The disadvantage of the operation is obvious in cases in which the growth from the upper tibial epiphysis has not yet ceased.

2. In the Goldthwaite operation the lateral half of the patellar tendon is detached and passed under the remainder, to be reinserted medially.

3. Gallie and LeMesurier tethered the patella to the medial femoral condyle by a sling of *fascia lata* passed through drill holes in the two bones.

4. Krogius devised a "capsular plasty", in which an ellipse of fascia is removed from the medial aspect of the joint and used as a graft to widen the lateral aspect.

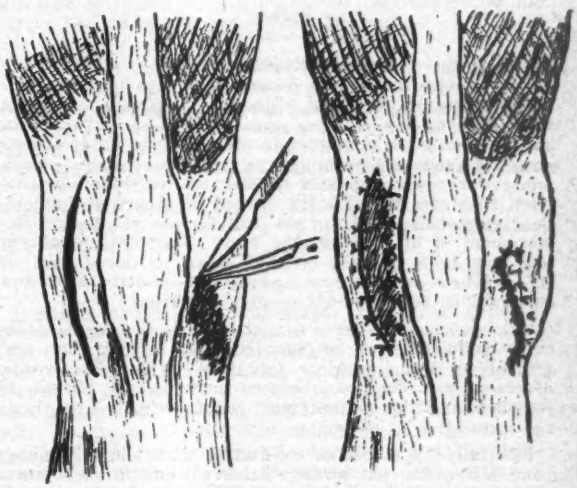

FIGURE I.

5. Albee treated patients in whom the lateral femoral condyle was deficient by making a cut with an osteotome, lifting the condyle forwards and inserting a bone block to maintain its new position.

6. The method for post-traumatic dislocation is the performance of a capsular plasty, which is similar to the Krogius operation in principle, but while it is more extensive in scope, it is simpler. The knee joint is exposed by a large lateral incision of the Kocher type, and attention is directed to the scarred mass of tissue which connects the patella to the lateral surfaces of the tibia and

[1] Read at the annual meeting of the Australian Orthopædic Association, Hobart, September 9 to 12, 1953.

fibula, which is the offending lesion, and this is divided and as much as possible removed until the bias to pull the patella laterally is removed. This usually involves opening the joint. Then a long parapatellar incision is made on the medial side of the capsule, about two centimetres medially. The outer edge is passed under the inner edge, and this incision in the capsule is closed so that the two layers overlap. The incision in the outer side of the joint is then closed *secundum artem* or left open, and the wound is closed over it. Knee flexion is commenced when the wound has healed, and is usually limited at first, but gradually increases. This operation has corrected the condition in cases in which previous transplantation of the insertion of the patellar tendon had failed.

Summary.

In cases in which the patella becomes dislocated from malalignment or capsular laxity, operations to realign the patellar tendon may suffice. Many patients are cured by physiotherapy alone. In post-traumatic cases laxity is not a feature, and the condition is caused by precisely the opposite circumstances — that is to say, rigidity from cicatricial tightness in an area bounded by the lateral aspect of the patella, the upper lateral surface of the tibia, the biceps tendon and the metaphyseal region of the femur. Flexion of the knee is possible only by yielding of a corresponding area medial to the patella, which permits the femoral condyles, so to speak, to "herniate" through. The rational way of treating the condition is therefore to remove the cause by the Krogius operation or the modification described.

THE SURGICAL TREATMENT OF TUBERCULOUS JOINTS.[1]

By F. H. McCLEMENTS CALLOW,
Sydney.

THE object of treatment of any condition must always be the restoration of the damaged part to normal, both in form and in function. In the treatment of joints affected by tuberculosis the restoration to normal function has not been often attempted for many years: bitter experience had shown that attempts to obtain movement in such joints were often followed by disaster, so that a patient often spent years of his life in bed or otherwise immobilized, and the reward for his patience was the loss of the movement of his joint at the best. This state of affairs has now been altered, largely owing to the arrival of three drugs—streptomycin, paraamino-salicylic acid and iso-nicotinic acid hydrazide—and operation.

The essential difference is that with these drugs a tuberculous joint may now be regarded as an infected joint and treated on basic surgical principles. In other words, abscesses are drained, diseased and necrotic tissue is removed, and the patient may, when treated early, hope for restoration of movement in the joint.

Naturally we are often confronted with joints in which bone destruction has already occurred, and in such joints there are mechanical factors which will interfere with movement even if the disease is completely eradicated.

The plan of treatment is simple and is based on constitutional treatment on generally accepted lines. As soon as the diagnosis is made, treatment with streptomycin and paraamino-salicylic acid is commenced; but in many cases no particular improvement is noted. The reason for this is that tuberculosis is a cold disease and is characterized by ischæmic necrosis instead of the hyperæmia found in most inflammatory conditions, and it is essential to remember that this avascularity, due to an obliterating endarteritis, is characteristic of the pathological changes, so that the antibiotic is unable to gain access to the main affected area in effective concentration. If this ischæmia can be changed to hyperæmia, then streptomycin and its allies can get to work and improvement may be expected. This has been noticed on several occasions when a patient with discharging sinuses has become secondarily infected and the pathological picture changed to hyperæmia in the surrounding tissues. The change in these cases may be absolutely dramatic. With conservative treatment and streptomycin the prognosis is better for the patient with infected sinuses than for the patient with intact skin.

Operation is designed to destroy the mechanical barrier and to cause hyperæmia, so that in addition to the removal of diseased tissue it allows the antibiotic to reach the seat of the trouble. Operation consists of wide removal of diseased synovial membrane. Necrotic bone, if present, is removed and débris is curetted away. Two grammes of streptomycin in powder form are put in the wound, which is then closed. A splint is applied to rest the joint and, of course, general treatment is continued. Splinting is maintained while the joint shows signs of inflammation and muscle spasm, and it is discarded as soon as these disappear. Movement is then allowed, but of course not forced. The surgeon must watch closely for any evidence of reactivation of the disease which would demand more rest.

There is evidence which indicates that consolidation and repair of bone will not occur in the presence of pus, particularly in the spine; this almost certainly accounts for the heart-breaking progress of the disease in the thoracic area in children, with its increasing destruction and deformity. We consider, therefore, that all tuberculous abscesses should be evacuated. In the spine this procedure generally requires a costo-transversectomy, which may be extended to an antero-lateral decompression when necessary, and the latter is imperative when paraplegia is present.

So far, our series of cases is so small that analysis is useless and only an impression can be gained; but we have seen tuberculous joints regain full movement when treated early. In one later case, in which there was considerable bone destruction, the hip was cleaned out and the head of the femur removed; some months later, when the hip was reopened, the condition was so good that, instead of its being fused, an acrylic prosthesis was fitted and a satisfactory range of painless movement resulted.

Detailed reports of end results have been published by other surgeons in sufficient numbers to demand attention, and these indicate that the period of disability in surgical tuberculosis may be reduced from years to months.

[1] Read at the annual meeting of the Australian Orthopædic Association, Hobart, September 9 to 12, 1953.

DELAYED POST-OPERATIVE RECURARIZATION.

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IN many centres most major surgery is now performed under endotracheal anæsthesia with the use of relaxing agents with a curare-like effect. This technique affords good surgical relaxation under light anæsthesia and is pleasant for the patient, having a rapid induction and few after-effects. However, the increasing complexities of modern anæsthesia necessitate a thorough knowledge of the dangers inherent in the newer methods and drugs, so that grave and perhaps fatal complications may be avoided.

The most frequently used technique is endotracheal intubation after induction of anæsthesia with thiopentone given intravenously and a relaxing agent. The anæsthetic is then continued with a closed-circuit absorption technique

[1] Working with the aid of a grant from the National Health and Medical Research Council, Commonwealth of Australia.
[2] Drug Houses of Australia Research Fellow in Medicine.

in which nitrous oxide and oxygen are used, supplementary doses of thiopentone and relaxants being given as required by the tolerance of the patient and the duration of operation. The patient remains curarized throughout the operation, and respiration is maintained artificially.

The relaxing agent commonly used is 1:2:3:tri-(2-diethylaminoethoxy) benzene triethiodide (gallamine triethiodide, "Flaxedil"). This is a drug which produces paralysis of voluntary muscle by antagonizing the action of acetylcholine at the myo-neural junction. It resembles d-tubocurarine in its action, but differs in having little effect on transmission of the nerve impulse in autonomic ganglia, and no histamine-like action, although it has a vagolytic effect. It is not broken down in the body, but is largely excreted unchanged in the urine within two hours of intravenous injection (British Pharmaceutical Codex Supplement, 1952). In man the usual initial dose is 80 to 120 milligrammes given by intravenous injection, though larger doses may sometimes be needed. It produces complete curarization in three to four minutes, and this lasts for thirty to forty minutes depending on individual tolerance.

Curarization has usually disappeared at the end of the operation, and the patient is breathing normally without assistance from the anæsthetist. This is not always so, and occasionally the patient is still curarized at the end of the operation. When this happens the effects of gallamine triethiodide are annulled by neostigmine, which is given intravenously in doses of up to 5·0 milligrammes. Neostigmine allows the accumulation of acetylcholine at nerve endings by inactivating choline esterase. It thus antagonizes the curariform effects of gallamine triethiodide. It has also side-effects due to stimulation of autonomic ganglia—contraction of smooth muscle, cardiac inhibition and glandular secretion. These are minimized in anæsthetic practice by giving atropine (0·5 to 1·0 milligramme) intravenously about ten minutes before the neostigmine.

It is currently believed and taught that no further danger of respiratory distress from curarization due to gallamine triethiodide is possible after spontaneous respiration has been restored by the administration of neostigmine. We have recently seen a group of patients in whom this was not so, for they appeared to show a delayed curare effect after a latent period of apparently normal respiration. It is the purpose of this paper to report these cases and so draw attention to this late anæsthetic complication which we have termed "delayed post-operative recurarization".

Case I.

A male patient, aged fifty-one years, had a chronic duodenal ulcer for which antroduodenectomy was performed. He had no evidence of cardio-renal disease, his nutrition was good, and his weight was 138 pounds.

The anæsthetic agents used were nitrous oxide and oxygen, given by the endotracheal route after induction with thiopentone and "Flaxedil". A total of 300 milligrammes of "Flaxedil" was given during the operation, which lasted for three hours, and 1·0 milligramme of atropine and 3·5 milligrammes of neostigmine were given at the end of the operation. His condition was good throughout operation, and his systolic blood pressure was 160 millimetres of mercury when he left the operating theatre. At no stage had he been cyanosed. When examined shortly afterwards in the ward he was slightly cyanosed with gasping respirations, but soon improved and became alert and able to talk coherently.

Forty minutes later a nurse found the patient cyanosed and semi-comatose. A definite tracheal tug with paradoxical respiration and generalized muscular hypotonia were present.

An injection of one milligramme of "Prostigmin" was given intravenously, and within thirty seconds the patient improved dramatically, with a disappearance of the paradoxical respiration and a return to normal colour. He then complained of an inability to breathe and asked to be sat up fully. He became restless and difficult to restrain and tended to overbreathe. The blood pressure had fallen to the pre-operative level of 130 millimetres of mercury, systolic. Despite the over-all improvement his jaw tended to drop, with a falling back of the tongue causing minor obstruction, and half an hour later a further 0·5 milligramme of "Prostigmin" was given with benefit.

The next day the patient was well and had no recollection of the episode. He made an uneventful recovery.

Comment.

In this case we have little doubt that the patient was suffering from delayed post-operative recurarization, for the clinical signs shown by him and the dramatic recovery after administration of neostigmine strongly support this diagnosis. It is probable, too, that a minor degree of curarization was present when the patient left the operating theatre.

Case II.

A male patient, aged sixty years, developed right apical empyema after pneumonectomy for carcinoma of the lung.

A right apical thoracoplasty was performed. Anæsthesia was induced with thiopentone and "Flaxedil", and continued with nitrous oxide and oxygen given by the endotracheal route. Atropine and "Prostigmin" were administered at the completion of the operation, although the exact doses of drugs given have not been recorded. The patient's condition was considered to be satisfactory when he returned to the ward. He was able to talk. He was placed in an oxygen tent, which is a routine procedure for patients having this operation in this hospital.

One hour after operation, whilst still in the oxygen tent, he developed cyanosis and respiratory distress and his respiration rate fell to eight per minute. His pulse rate was 140 per minute, and his blood pressure 180 millimetres of mercury, systolic, and 110 millimetres, diastolic. A diagnosis was made of delayed post-operative recurarization, and atropine (0·65 milligramme) and "Prostigmin" (2·5 milligrammes) were given by intravenous injection. Within two minutes, without further treatment, his respiration rate rose to 18 per minute, his colour returned to normal and he had no further respiratory distress.

Comment.

This patient also had the syndrome of delayed post-operative recurarization. He developed respiratory distress responding to neostigmine after a latent period of normal respiration. Diminution of the vital capacity and paradoxical respiration (which follows thoracoplasty) may also have been contributing factors. The uselessness of oxygen administration without further measures in this condition is well shown by this patient, for he developed respiratory distress while actually in an oxygen tent.

Case III.

A female patient, aged thirty-four years, had a pyelolithotomy for a staghorn calculus in the left kidney. The right kidney had been removed for nephrolithiasis two years previously. Her condition was fair before operation, there being no evidence of cardiac or vascular disease. The blood urea content was 42 milligrammes per 100 millilitres.

An endotracheal tube was passed after induction of anæsthesia with 0·5 gramme of thiopentone and 120 milligrammes of "Flaxedil", and the anæsthetic was continued with nitrous oxide and oxygen. A further 120 milligrammes of "Flaxedil" (making a total dose of 240 milligrammes) were given during the operation, which lasted for eighty minutes. No neostigmine was required to reestablish spontaneous respiration.

For two hours after operation the patient was in fair condition and maintained her pulse and respiratory rates and blood pressure at pre-operative levels. At this stage, however, she developed non-coordinated, jerky movements, muscular atony and dyspnœa. She complained of inability to breathe. Atropine (0·65 milligramme) and neostigmine (2·5 milligrammes) were given with rapid improvement.

She was discharged from hospital in good health twenty-eight days after operation.

Comment.

This patient developed acute respiratory insufficiency after a period of apparently normal breathing and was rapidly relieved by neostigmine. In this case renal damage and oliguria may have contributed to the development of delayed post-operative recurarization.

Case IV.

A male patient, aged fifty-four years, developed a recurrent gastro-colic fistula which required operative repair. He had no evidence of cardiac or renal disease. Weight loss was minimal, and there was no evidence of electrolyte disturbance prior to operation. His weight was 137 pounds.

A one-stage excision of the fistula and establishment of a colostomy were performed under endotracheal anæsthesia with nitrous oxide and oxygen, together with thiopentone given intravenously and "Pethidine". An initial dose of 160 milligrammes of "Flaxedil" was administered to permit intubation, and a further 120 milligrammes were administered during the two and a half hours' operation. At the end of the operation atropine and neostigmine (2·5 milligrammes) were given intravenously.

The patient returned to the ward apparently in good condition, with his pulse rate and blood pressure at pre-operative levels. He had no respiratory distress, and there was no cyanosis or sweating. He was able to converse intelligently.

Quite suddenly, two and a quarter hours after operation, his respirations became slow, irregular and gasping, and he lapsed into coma. His pulse had ceased by the time medical aid arrived.

Post-mortem examination showed that atheroma was present to some degree, although in the heart and brain no infarction or hæmorrhage was macroscopically evident. There was no evidence of perforation or hæmorrhage in the abdomen. The lower lobes of both lungs were collapsed, and microscopic examination revealed capillary congestion and alveolar exudate.

Comment.

This patient was seen before we were aware of the possibility of delayed post-operative recurarization, but the clinical picture and pathological findings suggest in retrospect that this may have contributed to his death. At the time, death was thought to be due to cerebral atheroma with infarction, leading to cardio-respiratory failure. Gastro-colic fistulæ are also notoriously prone to produce subtle biochemical changes.

Discussion.

These patients all received large doses of gallamine triethiodide as part of an anæsthetic for a major surgical procedure. They appeared to be in good condition before and at the end of operation, but developed acute respiratory distress after a latent period of apparently normal breathing. This respiratory distress responded to neostigmine. No patient had any clinical or laboratory evidence of hæmorrhage, shock, electrolyte upset, cardiac insufficiency or cerebral disease.

The symptoms and signs exhibited by these patients strikingly resemble those of curarization. This symptomatology, the response to neostigmine and the failure to respond to other therapy, and the absence of any other discernible cause of respiratory collapse, leave little doubt that these patients did in fact suffer from delayed post-operative recurarization.

The clinical picture of delayed post-operative recurarization is distinctive and should be recognized, for specific treatment with neostigmine is both simple and dramatically efficacious. The syndrome is seen in patients who receive prolonged anæsthesia with relaxant drugs. They are in good condition at the end of the operation, and return from the operating theatre to the ward breathing spontaneously with good colour and adequate circulation. This, however, does not exclude the presence of a minor degree of curarization at the end of the operation (Case I) leading to early muscular fatigue.

The relaxant used in the cases reported here was gallamine triethiodide ("Flaxedil") given in high dosage, of the order of 240 to 300 milligrammes for an operation lasting up to three hours. In three of four cases, atropine and neostigmine were required to reestablish spontaneous respiration after operation.

After an interval of normal respiration, varying from forty minutes to just over two hours, the patients have developed acute respiratory distress.

The onset of respiratory distress is rapid. The patient complains of inability to breathe. This is followed by progressive paresis, non-coordinated jerking movements, cyanosis, sweating, circulatory failure, coma, and death from anoxia. The paresis affects first the muscles of the head and neck, so that the patient has ptosis and cannot wrinkle his forehead or support his tongue or jaw. The muscles of the limbs are next affected, then the intercostals and lastly the diaphragm. The respiration rate is slow and irregular, but the pulse rate and blood pressure are maintained until anoxia supervenes. This sequence is almost exactly that seen in curarization.

Delayed post-operative recurarization can be largely avoided by the use of minimal doses of relaxant, especially towards the end of operation and in patients with cardiac or renal disease. The treatment of the established condition is both simple and efficient, for neostigmine given in doses of up to 5·0 milligrammes by intravenous injection is specific. Should neostigmine be unavailable, the patient will recover eventually if an adequate respiratory exchange is maintained until the curariform effect of the drug wears off. This requires artificial respiration and maintenance of a clear airway. Oxygen therapy by itself is of little value. Indeed, in one of the present cases (Case II), delayed recurarization occurred in a patient whilst he was in an oxygen tent.

The pathogenesis of this syndrome is not precisely known, but several factors are involved. In all cases to date a high dose of "Flaxedil" (240 milligrammes or more) has been used. In three cases neostigmine was given to restore normal breathing. Cardio-respiratory and renal disease may be contributing factors, as was seen in Cases II and III. Renal disease is especially important, for gallamine triethiodide is not metabolized by man but eliminated by renal excretion. If urinary excretion is low, the gallamine triethiodide will be retained in the body. Thus a patient with primary renal disease (Case III), or with poor urinary output from some other cause, such as dehydration or hæmorrhage, may be curarized for long periods from relatively small doses of relaxant, and require neostigmine to begin spontaneous respiration. The fate of neostigmine in man is less certainly known, but there is evidence that it can be inactivated by mammalian tissues (Beckman, 1952). Should the neostigmine be eliminated more rapidly than the relaxant, delayed recurarization may take place.

A second mechanism is muscular fatigue. A patient able to breathe spontaneously for short periods may still be lightly curarized, and prone to muscle fatigue (Case I). This also could lead to delayed respiratory failure. After the administration of respiratory depressants such as thiopentone or "Omnopon", the clinical detection of minor degrees of curarization is extremely difficult.

Summary and Conclusions.

Four cases are reported in which a presumptive diagnosis was made of "delayed post-operative recurarization". This syndrome consists of acute respiratory distress after a latent period of up to three hours following an anæsthetic in which gallamine triethiodide has been used. The symptoms and signs are those of curarization, and there is a rapid response to neostigmine. Renal disease and muscular fatigue may be contributing factors in the pathogenesis.

It is suggested that delayed post-operative recurarization is a possible cause of respiratory failure and even death in the hours following an anæsthetic and use of relaxant drugs, although the patient has been breathing spontaneously after apparent recovery from anæsthesia.

Acknowledgements.

We wish to thank those members of the honorary medical staff who had these patients under their care for permission to quote these case reports. We are also deeply grateful to many of our senior colleagues for advice and constructive criticism.

References.

BECKMAN, H. (1953), "Pharmacology in Clinical Practice", Philadelphia and London: 121.

BRITISH PHARMACEUTICAL CODEX SUPPLEMENT (1952), London: 30.

THYROID SYMPOSIUM II: PROTEIN-BOUND IODINE AS DIAGNOSTIC AID IN THYROID DYSFUNCTION.[1]

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THE clinical manifestations of even apparent hyperthyroidism or myxœdema often present diagnostic problems. When complicating or confusing symptoms are present, as is often the case, the true evaluation of thyroid activity requires more extensive investigation.

The most commonly used basal metabolic rate is often misleading, and being only a measure of oxygen consumption (the result of various oxidative processes in the body) cannot be regarded as a direct indication of the rate of production and utilization of thyroid hormone. The blood cholesterol content, often useful in cases of myxœdema, is of no value in thyrotoxicosis.

A number of methods employing radioactive iodine (I^{131}) for evaluation of thyroid function are in existence. They are based on the thyroidal uptake and/or urinary excretion rates and more recently on thyroid clearance studies involving the level of total radio-iodine in the blood, or of protein-bound radio-iodine (PBI^{131}).

Although their diagnostic value has been well established and the techniques have been greatly simplified, they still require the administration of the radioactive isotope, which is not always practicable in this country.

An alternative is the biochemical assay of the inert circulating blood iodine I^{127}.

During the last decade ample evidence has been accumulated to show that the plasma "protein-bound iodine" or "serum precipitable iodine" fraction represents the metabolically active circulating hormone—thyroxine (Taurog and Chaikoff, 1948) and tri-iodothyronine (Gross and Pitt-Rivers, 1952, 1953)—and that its concentration in blood is a very reliable index of thyroid activity (see Tables I and II). The values characteristic of myxœdema are below and those of hyperthyroidism above the euthyroid range (Rapport and Curtis, 1950). After successful therapy, with thyroid preparations in the case of the former, and operation or the administration of antithyroid drugs or radioactive iodine in the latter, they revert to the normal level.

The normal range for the euthyroid state has been generally accepted as from four to eight microgrammes per 100 millilitres (Riggs and Man, 1940; Starr *et alii*, 1950; Tucker and Keys, 1951; Kydd *et alii*, 1950). It varies somewhat for different methods (Zak *et alii*, 1953), geographical position (Rapport and Curtis, 1950) and food habits (Fertman and Curtis, 1951). There is also a certain degree of overlap in borderline cases, in which the normal and abnormal cannot be clearly separated. These, however, do not comprise more than 10% of all the cases. Moreover, the mean value for the normal range, as quoted by different authors, is surprisingly constant (see Table III).

The diagnostic value of PBI estimations is based on the stability of this iodine fraction in health and in non-thyroid disease. It is not influenced by exercise or food intake (Starr *et alii*, 1950), except when sea foods rich in iodine are ingested. Obesity does not affect it (Williams, 1948; Starr *et alii*, 1950). Day-to-day and seasonal variations are slight, and there is no apparent difference between the sexes, although the menstrual cycle may cause slight variations (Rapport and Curtis, 1950). The few exceptions are as follows: (*a*) in old age, in which the downward trend in PBI values is attributed to diminished requirements of peripheral tissues (Tucker and Keys, 1951; Perlmutter and Riggs, 1949); (*b*) during gestation, when a rise of PBI level (Winkler, 1947) not later than in the first four weeks is supposed, according to Man *et alii* (1951), to be essential for the successful termination of pregnancy; (*c*) in rare cases of a non-thyroid disease, as in infective hepatitis, when a rise in PBI level frequently occurs (Kydd and Man, 1951).

DIAGNOSIS	BMR	PBI (SERUM)	RAI (UPTAKE)
NORMAL OR EUTHYROID	↔	↔	↔
THYROTOXICOSIS OF GRAVES' DISEASE	↑	↑	↑
THYROID ADENOMA WITH HYPERTHYROIDISM	↑	↑	↑
HYPERTHYROIDISM PERSISTING ON IODINE	↑	↑	↓
HYPERTHYROIDISM FACTITIA	↑	↑	↓
HYPEROPHTHALMOPATHIC GRAVES' WITH EUTHYROIDISM	↔	↔	↔
PRIMARY MYXEDEMA	↓	↓	↓
PITUITARY MYXEDEMA	↓	↓	↓
IODINE WANT	↔	↔	↑
END-ORGAN INSENSITIVITY TO THYROID HORMONE (THEORETICAL)	↓	↑	?

TABLE I.

Basal metabolic rate, PBI value and radioactive iodine uptake in thyroid disorders. (From Means, 1950.)

In certain diseases of the thyroid gland, however, when the functional state of the gland has not been disturbed by the prevailing pathological conditions, the PBI level remains within the euthyroid limits—for example, non-differentiated carcinomata, non-toxic adenomata, thyroiditis (Rapport and Curtis, 1950).

A serious limitation to the diagnostic value of the PBI estimation is the effect of various medications administered to the patient. Some of them can cause a spurious elevation of PBI level, while the real "hormonal iodine" fraction remains unchanged, as shown by butanol extraction procedures (Man *et alii*, 1951); others, by temporarily suppressing thyroid activity, do not give a true picture of the gland's function.

[1] Part I of this symposium, entitled "Radio-Active Iodine (I^{131}) and Protein-Bound Iodine in Thyroid Disorders", by J. P. Madigan and W. E. King, was published in the issue of May 29, 1954.

The first category comprises the following: iodides and Lugol's solution (Danowski *et alii*, 1950; Danowski, Johnston and Greenman, 1950), tincture of iodine, thyroid preparation (Danowski *et alii*, 1952), iodized salt, cough mixture and throat tablets, and opaque dyes used for X-ray examination (lipiodol, "Periodax", "Diodrast"), which give false high readings (Rapport and Curtis, 1950; Man *et alii*, 1951; Man and Peters, 1950; Hyde and Hyde, 1949). The second group causes a pronounced drop in PBI values: antithyroid drugs (Engstrom *et alii*, 1950; Hallman *et alii*, 1951), thiocyanate (Rapport and Curtis, 1950), mercurial diuretics (Meyers *et alii*, 1951), resorcinol, PAS, cortisone (Fredrickson *et alii*, 1952) and ACTH, excess of vegetables of the cabbage family (Fertman and Curtis, 1951), lack of iodine.

In most cases the false results can be avoided by allowing a suitable time interval to elapse after the therapy has been discontinued. This varies from a few days to a few months, or even to a few years, as after the injection of lipiodol. Unfortunately individual variations make it very difficult to adopt a routine procedure which would be satisfactory in every case. General recommendations are set out in the paper by Madigan and King (1954).

DIAGNOSIS	BMR	PBI (SERUM)	RAI UPTAKE
ANOREXIA NERVOSA	↓	↓	↓
STARVATION	↓	↓	↓
NON-MYXEDEMATOUS HYPOMETABOLISM	↓	↔	↔
HYPERMETABOLISM WITHOUT THYROTOXICOSIS	↑	↔	↔
DINITROPHENOL POISONING	↑	↓	↔
NEPHROSIS	↓	↓	↔
PREGNANCY	↑	↑	?
PHAEOCHROMOCYTOMA	↑	↔	↔
LEUKEMIA	↑	↔	↔
ADDISON'S DISEASE	↓	↔	↔

TABLE II.

Basal metabolic rate, PBI value and radioactive iodine uptake in non-thyroid disorders. (From Means, 1950.)

Materials and Methods.

The work presented in this paper is a part of an investigation carried out jointly at the Royal Melbourne Hospital, the Commonwealth X-Ray and Radium Laboratory and the Biochemistry Department of the University of Melbourne. Its object was to aid in establishing physical indices in tracer studies with I^{131} and at the same time to test the value of PBI estimations in diagnosis and treatment of thyroid disorders. Most of the patients who were tested for PBI values are listed in the paper by Madigan and King; in addition to these, however, a small number of cases are included which were not reviewed by the "panel", but came from various sources for PBI estimations only.

The blood samples were usually drawn concurrently with those taken for radioactive I^{131} studies (after an injection of a tracer dose). However, if the patient required more investigations or treatment with I^{131}, some additional blood samples were taken between two tracer tests or in intervals after the administration of a therapy dose, usually when the patients came for a routine check-up.

TABLE III.

Normal Range and Mean PBI Values for Euthyroid Individuals as Quoted by Various Authors.

Name of Author.	Date.	Number of Cases.	PBI Value. (Micrograms per 100 Millilitres.)	Range.
Salter, Bassett, Sappington	1941	10	5·2	4·6 to 5·9
Winkler	1947	235	5·8	0·5 to 17·4
Riggs	1947	55	5·1	3·5 to 7·5
Connor, Curtis and Swenson	1949	800	4·6	3·7 to 6·7
Perlmutter and Riggs ..	1949	16	4·8	3·6 to 6·4
Starr, Petit and Chaney ..	1950	100	5·5	4·0 to 8·5
Kydd, Man, and Peters ..	1950	80	5·4	3·8 to 7·8
Tucker and Keys ..	1951	402	5·8	2·6 to 11·0
Hallman, Bondy, Hagewood	1951	37	5·4	3·2 to 8·0
De Mowbray and Tickner ..	1952	30	5·0	4·0 to 8·0
Melbourne values	1951–53	106	5·1	2·7 to 8·0

Whenever possible a standardized diet of low iodine content was observed for a week to a fortnight preceding the test. This was done to ensure more uniform conditions for the test, and also to avoid a sudden flooding of the system with iodine. The diet sheet handed to the patients included also a list of drugs and miscellaneous items likely to influence the test.

The normal controls were mostly recruited from amongst the medical students and members of the staff. The donor was interviewed, and no sample was taken if the daily menu included sea foods taken twenty-four hours previously. This precaution proved necessary after a PBI estimation of a blood sample taken from one normal individual gave an iodine value of 13·5 micrograms per 100 millilitres three hours after a lunch consisting of a lobster salad.

Ten millilitres of blood obtained by venepuncture were placed in a dry oxalated centrifuge tube and mixed thoroughly. The plasma was separated as soon as possible (as Hallman *et alii*, 1951, found a rise in PBI value when the specimen was allowed to stand) and the analysis was completed within forty-eight hours.

Usually two or more blood samples were taken from each patient at intervals of one or two days. In view of our later experience with day-to-day variations, particularly in the toxic and borderline toxic group, this was necessary to get a true picture of the average hormonal output (which does not seem to be uniform for the hyperthyroid gland or in neurasthenia).

In many borderline cases, in which the clinical diagnosis was equivocal, it was most imperative to obtain a series of PBI values to indicate the trend of the fluctuations before deciding on the future management of the patient. In case of surgical procedure or after I^{131} therapy one sample of blood was taken at a time in order to check the progress of therapy or the effect of operation. If the PBI result was not in good agreement with the clinical data further tests were carried out.

We used Barker's distillation method (1948). The colorimetry was carried out in a Klett Summerson photoelectric colorimeter.

As the technique is extremely delicate and every laboratory using it develops its own small modifications suitable for local conditions, the following details may be of value.

Precipitation.

It is found that the precipitation is complete and the supernatant clear if the plasma is first pipetted and $ZnSO_4$ is added, and then after the addition of NaOH the mixing is done slowly with a "folding-in" motion. If the supernatant fluid is still cloudy, we add a few drops of the precipitated $Zn(OH)_2$, stir it up again and repeat the centrifuging.

Digestion.

Digestion is carried out on an electric heater with a thermometer inserted inside the flask. The mixture is heated to 185° C. the first time, and to 180° C. the second time. As controls we use reagents only, which remain very stable for each batch.

Distillation.

Different stills require various rates of heating and individual management. As all flasks are not exactly interchangeable, every set should be checked for recovery. Our results are corrected by +10%, as indicated by Barker. As trapping solution, 0·5 millilitre of a 1·5% arsenious oxide solution in N NaOH solution is used. The phosphorous acid is followed by 0·5 millilitre of 30% H_2O_2, which seems to give a lower "blank".

Colorimetric Procedure.

The bath is used at 37·0° C. ± 0·2° C. with a fifteen-minute incubation period, which allows up to 15 samples in duplicate to be estimated in each series. A standard solution of 0·05 microgramme of iodine in five millilitres is always included at the beginning and at the end of each batch. Reading is done within ten seconds, and a thirty-second interval is allowed between the two readings. Our main difficulty is the daily variation in room temperature (very pronounced in Melbourne), and therefore we allow only ten seconds for reading after removing the sample from the constant temperature bath.

A standard curve which has been found remarkably reproducible is used for calculating the quantities of iodine. Standard solutions keep almost indefinitely in a refrigerator.

Our range is as for solutions containing 0·01 to 0·1 microgramme of iodine in five millilitres. By prolonging the time of incubation to thirty minutes or cutting it to 7·5 minutes, we can estimate the concentration of iodine as low as 0·005 microgramme or as high as 0·2 microgramme in five millilitres respectively with a 5% to 8% error.

Our duplicates agree to within 0·2 to 1·0 microgramme *per centum*. For checking the recovery we use NaI added, before digestion, to a protein material consisting of two millilitres of a 5% (dry weight) solution of hæmoglobin in N NaOH solution. This keeps well and gives a low iodine reading. We recover from 95% to 100% (corrected) of added NaI, while blank readings (without the hæmoglobin) correspond to 0·013 to 0·025 microgramme of iodine in five millilitres, depending on the grades of sulphuric and phosphorous acids available. We consider chromic acid (Merck, United States of America) most suitable and use it directly. Sulphuric acid is purified with HCl as described by Barker, while the phosphorous acid (Standard Laboratories, England) is boiled for one hour with 0·5 millilitre of 30% H_2O_2 per 100 millilitres of acid.

We found that 20 millilitres of saturated solution of oxalic acid can be substituted for the phosphorous acid with satisfactory results. The procedure, however, is very cumbersome, and we used it only in emergency (that is, when phosphorous acid was not available).

Results.

As was previously stated, the series presented here includes PBI values obtained during the last two years from patients suspected of thyroid disorders and from normal controls. The results were clinically reliable, and duplicate estimations agreed to within one microgramme per 100 millilitres. If one value only was available, it was accepted, provided that it closely approximated the next day's sample; or in rare cases, when after one sample had been taken more blood was not available, it was also included, provided that the result was in good agreement with the clinical assessment and also with the physical indices.

The following groups of subjects are included: (i) normal controls; (ii) euthyroid subjects; (iii) hyperthyroid patients; (iv) hypothyroid patients (see Figure I). This classification has been made on the basis of the concurrent clinical assessment. In some cases, however, if the patient was reclassified, the final diagnosis was taken as a basis for comparison. Final diagnosis was arrived at after a careful scrutiny of the clinical data by the whole panel, as in some cases the results of therapy became apparent only after a time interval. If the panel could not reach an agreement, a second series of investigations was carried out.

Estimations of the basal metabolic rate proved to be very unreliable and were not taken into consideration for the final diagnosis.

Cases in which the preexisting medication was likely to influence the results are treated separately.

In cases in which the clinical assessment was indeterminate owing to lack of agreement between two or more clinical observers, or in which clinical assessment and PBI tests were not made concurrently, the results are omitted.

In this paper no attempt has been made to correlate the PBI values with physical indices. Comparison of uptake figures with PBI and forty-eight hour PBI^{131} values in various thyroid disorders will be published elsewhere.

Normal Controls.

A series of tests on apparently healthy individuals and on hospital patients without apparent thyroid disorders has been performed.

Since it has been found by American workers (Danowsky *et alii*, 1949; Connor *et alii*, 1949; Starr *et alii*, 1950) that the day-to-day fluctuations for healthy subjects were negligible, one sample only was taken from most of them. Out of the total number of 106, a group of 82 results from 81 healthy individuals was statistically examined. Of these, 77 (or 94%) fell within the values of 3·0 to 7·5 microgrammes per 100 millilitres of plasma. The mean was 5·1 microgrammes per 100 millilitres. Amongst values outside this range, one of 2·8 microgrammes per 100 millilitres, when the test was repeated some weeks later, rose to 4·7 microgrammes per 100 millilitres, while three others (which had to be finally excluded as representing single estimations) were above 7·7 microgrammes per 100 millilitres.

Definition of Normal Range.—The distribution of values has been statistically examined and proved to be as for a normal population. Moreover, it was proved that the normal controls and the group of euthyroid subjects have the same distribution; otherwise there is no difference between the PBI values of euthyroid patients and those of normal controls, and the chances are 1000:1 that 95% of the PBI values in both of these categories will fall between 2·7 and 8·0 microgrammes per 100 millilitres and 90·5% between 3·0 and 7·5 microgrammes per 100 millilitres. The figures of 2·7 microgrammes per 100 millilitres and 8·0 microgrammes per 100 millilitres have been accepted as boundaries above and below which no more than the stated percentage of normal persons will fall.[1] As, however, some

[1] These limits are obtained with the help of the assumption that the square root of the PBI value amongst the clinically normal persons has the Gaussian normal distribution. This assumption was confirmed statistically.

of the hypothyroid and hyperthyroid groups respectively had PBI values between 2·7 and 3·0 microgrammes per 100 millilitres and 7·5 and 8·0 microgrammes per 100 millilitres, these two ranges had to be considered as borderline where the normal and abnormal values overlap. Moreover, because of the daily fluctuations in PBI output in these groups, a single sample is not regarded as sufficient to permit a definition of borderline normal or borderline toxic or myxœdematous.

If the same normal distribution of the PBI value in the hyperthyroid group is also assumed as in the control group, the line of demarcation of 8·0 microgrammes per 100 millilitres will give the expected misclassification of 9·5% for both groups. The hypothyroid group was not large enough to permit a similar statistical test.

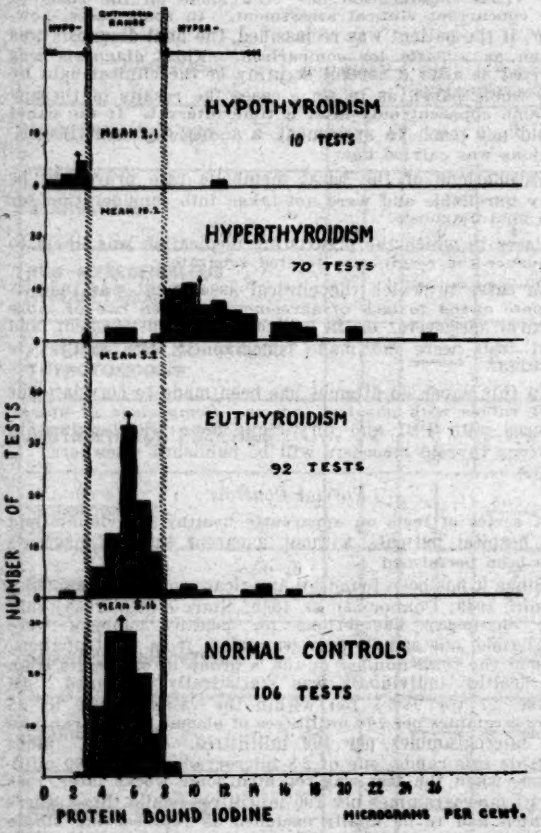

FIGURE I.

PBI distribution histograms in normal controls and in euthyroid, hyperthyroid and hypothyroid patients (Melbourne).

Euthyroid Group.

Results in the euthyroid group include PBI values estimated on patients reviewed by the panel and pronounced euthyroid. In all these patients a primary thyroid disorder or a secondary thyroid dysfunction accompanying other endocrine disease was suspected.

A number of results are included from patients who became euthyroid after treatment with antithyroid drugs or radioactive iodine or after surgical procedure. A temporary remission was also listed here if confirmed by clinical assessment. In addition, a few patients outside the panel are included. A wide variety of illnesses was represented, such as non-toxic colloid goitre, malignant exophthalmos, thyroid carcinoma, Hashimoto's disease, acromegaly, hypogonadism, pituitary dwarfism, *myasthenia gravis*, Cushing's syndrome, *diabetes mellitus*, neurasthenia, congestive heart failure and others.

Although most of these patients had some symptoms suggesting thyrotoxicosis or myxœdema, they have been pronounced clinically euthyroid *ab initio* or reclassified as such after a careful follow-up investigation. The clinical diagnosis in many cases was not a simple matter.

The series includes results of 92 PBI tests on 74 patients. Out of these, 34 are results of analysis of a single blood sample in duplicate, while 58 represent a mean value of two or more estimations on day-to-day samples in order to minimize daily differences and to obtain a more accurate picture of the thyroid function.

The validity of this procedure (taking the mean value of several estimations) has been confirmed by statistical analysis of a sufficient number of values representing results from all groups.

It proved that the error introduced by inaccuracy of duplicate estimations was negligible compared with the day-to-day fluctuations in PBI values of the same patient. These fluctuations were again insignificant compared with the difference between the average PBI values of individual patients, even of the patients belonging to the same category of illness. Consequently, when the differences between patients due to categories (illnesses) are being tested, the variation between the patients in the same category must be taken as a basis for comparison.[1]

The mean PBI values obtained in 83 out of 92 tests were as from 2·8 to 7·7 microgrammes per 100 millilitres, that is, within the normal range—in other words, 91% agreement with the clinical diagnosis. Out of these, four were borderline values. The mean arithmetical value for the whole group was 5·2 microgrammes per 100 millilitres, essentially the same as for normal controls.

Definition of Borderline Cases.—We regard a case as equivocal or borderline when the mean PBI value is in one of the overlap zones—that is, between 2·7 to 3·0 and 7·5 to 8·0 microgrammes per 100 millilitres. (This opinion is justified on the grounds of the above-mentioned statistical analysis, which showed with near certainty that only 4% approximately of the clinically normal persons have PBI values falling in each of these ranges.) Furthermore, even when the arithmetical mean indicates the euthyroid state—for example, successive PBI values being 6·6, 8·0 and 6·6 microgrammes per 100 millilitres, mean 7·4 microgrammes per 100 millilitres—we consider these large day-to-day fluctuations significant to such an extent that if the highest reading exceeds 8·0 microgrammes per 100 millilitres, the patient is regarded as a potentially hyperthyroid individual.[2]

The nine PBI values outside the normal limits were obtained from five patients. Four of these were single sample analyses. Three single tests on a patient originally classified as in a toxic state, who after a therapy dose of I^{131} became "clinically euthyroid", gave results still in the toxic range, but progressively decreasing—13·1, 10·1, 8·8 microgrammes per 100 millilitres—over a period of a few months. The other single sample test result was in the myxœdema range—1·8 microgrammes per 100 millilitres. The patient had congestive heart failure and œdema (increased iodine space?) and was taking "Neptal" (mercurial diuretic) shortly before the test.

The remaining six misclassified results (all but one of them being mean values of two or three day-to-day samples) came from three patients. One was from a patient with infective hepatitis. This condition, according to Kydd and Man (1951), is in its early stages accompanied by an elevated PBI value. The second was from a case of acromegaly, in which PBI values fluctuated widely from 2·5 to 17·6 microgrammes per 100 millilitres during three consecutive days. The toxic mean value is completely

[1] This part of the statistician's report was based on the hierarchic analysis of variance.

[2] Further statistical analysis will be carried out to clarify this point.

inconclusive in this case, as the fluctuations indicate either an erratic hormone production or an erratic hormone utilization, or both. The patient did not display any toxic symptoms, but had an elevated basal metabolic rate. De Mowbray and Tickner (1952) have described a similar result obtained from a patient with acromegaly, and the obvious conclusion is that PBI estimations are of no value in this condition.

The other three abnormal mean PBI values—ranging from 8·7 to 16·7 microgrammes per 100 millilitres—were results of nine analyses carried out on a clinically euthyroid young male who was originally classified as myxœdematous. As all these values were consistently in the toxic range, and in the absence of any known medication, no reason can be given for the lack of agreement with the clinical data. The suggestion of "end organ insensitivity" offered by Means (1950) is possibly the only explanation. The basal metabolic rate ranged from −29% to +8%.

It is intended to follow up this patient and study the "inorganic", "total" and "thyroxine" iodine alongside the PBI.

The basal metabolic rate in this group ranged from −20% to +45%.

Hyperthyroid Group.

The hyperthyroid group includes PBI values from patients with toxic diffuse or nodular goitre with or without exophthalmos, and from those with thyrocardiac symptoms. They were submitted to the panel for the purpose of diagnosis or treatment with I^{131}. Some cases of recurrent post-operative thyrotoxicosis were also included. All these patients have been pronounced in a toxic state clinically or so reclassified after careful study. In this group also, as for the euthyroid subjects, a number of borderline patients with equivocal symptoms are present.

During treatment with I^{131} a series of single samples at proper time intervals was taken for PBI tests to check the progress of therapy. A corresponding clinical assessment was usually made and the results were reviewed by the panel.

In case of antithyroid drugs being administered, a period of not less than three weeks was observed between the cessation of therapy and the test. In some cases, however, this time interval, which is sufficient for the majority of cases, proved not long enough, and the results obtained were not reliable and the tests had to be repeated.

This series consists of 70 tests on 40 patients; 15 are results obtained on a single sample, while the remainder are mean values of two or more tests obtained on day-to-day samples.

The PBI value in 64 out of 70 tests was in the range of 7·5 to 20·6 microgrammes per 100 millilitres, mean 10·2 microgrammes per 100 millilitres—90% agreement. Out of these patients, seven were in a borderline toxic state.

The first of the above-mentioned subgroup of six results was a PBI value of 2·5 microgrammes per 100 millilitres (mean of three estimations) obtained from a patient who had been for four weeks off thiouracil therapy of one year's duration and still exhibited toxic symptoms. Apparently a four-week interval was not sufficient in this case and the effect of the drug still persisted. The PBI value rose to 5·0 microgrammes per 100 millilitres a few weeks later without any clinical change.

A similar problem is presented by another patient with a PBI value of 4·0 microgrammes per 100 millilitres (mean value), who had been for four weeks off thiouracil therapy. In this case, however, even the clinical assessment was "euthyroid", and the final diagnosis, "toxic", was based on the patient's history and on physical indices.

A clinical assessment of "slightly toxic" was given in the third case, in which the mean PBI value was 7·3 microgrammes per 100 millilitres. Physical indices were inconclusive, and the same patient on being subsequently tested was classified as having a "non-toxic colloid goitre". An almost identical picture was presented in the next case, in which the mean PBI value was 5·8 microgrammes per 100 millilitres. Here the clinical assessment was "at most mildly toxic", and physical indices were within normal limits. It is quite obvious that the third and fourth cases were clinically borderline and required more extensive study.

In the fifth case, in which the PBI value was 4·4 microgrammes per 100 millilitres (single estimation), the test was carried out four weeks after a therapy dose and might have represented a transitional remission. The patient was still in a toxic state four months later, but subsequently became euthyroid.

The last non-toxic PBI value of 5·0 microgrammes per 100 millilitres (single sample) was obtained from a patient in a mildly toxic state with pretibial myxœdema after an I^{131} therapy dose four weeks previously. After withdrawal of covering thiouracil therapy the PBI value failed to rise although clinical symptoms indicated a toxic state. Four weeks later, however, the patient became "myxœdematous" clinically, and the PBI value fell to 2·8 microgrammes per 100 millilitres. In this case the previous "false" PBI value, far from being a failure, clearly indicated the change of thyroid function from toxic to euthyroid and then to hypothyroid.

All these results are included in this group for the purpose of assessing the validity of a random result of a test for PBI value without paying much attention to previous medication and clinical "borderline state". It is obvious that a single sample is not enough for the purpose of diagnosis and can often be misleading when taken during treatment, as a change in PBI value can often forestall clinical symptoms (Hallman *et alii*, 1951).

Furthermore, no evaluation of the degree of toxicity can be deduced from the PBI figure. Finally, a fall of PBI value within the toxic range does not always closely parallel clinical improvement unless it reaches a euthyroid value.

Hypothyroid Group.

The hypothyroid group includes a small number of only 10 cases of primary or secondary myxœdema. The PBI value was in the hypothyroid range—2·1 to 2·4 microgrammes per 100 millilitres—in seven cases, and in the borderline myxœdema range—2·8 to 2·9 microgrammes per 100 millilitres—in two cases. (The mean group PBI value was 2·1 microgrammes per 100 millilitres.)

The last case is the one of probable "end organ insensitivity" described in the euthyroid group, which during the first test was classified as a case of juvenile myxœdema. The mean PBI value representing the average of three estimations was 11·5 microgrammes per 100 millilitres.

The number of cases was too small for statistical analysis.

Medication.

The greatest difficulty was the interpretation of the results of tests when known or suspected medication was likely to interfere with the thyroid function or influence the technique of PBI estimation. In the group classified as hyperthyroid on clinical grounds, the mean PBI values ranged from 1·5 to 28·0 microgrammes per 100 millilitres when the thiouracil and/or Lugol's solution was administered, and from 3·3 to 9·5 microgrammes per 100 millilitres on thyroid preparations or mercurial diuretics. In 16 tests performed on 13 patients, the only useful conclusion which could be drawn was that if the patient still maintained an elevated PBI value in spite of the administered thiouracil medication, he could certainly be pronounced as "toxic". After the administration of Lugol's solution, iodide or thyroid preparations, on the other hand, no such conclusion could be drawn. In the clinically euthyroid group the mean PBI values in 11 tests on seven patients ranged from 5·2 to 56·5 microgrammes per 100 millilitres after Lugol's solution, lipiodol iodine, dye used for intravenous pyelography or thyroid preparations. A large number of tests performed on patients receiving interfering medication had to be omitted altogether in view of the indeterminate clinical diagnosis.

We found a PBI value of 62·7, 50·0 and 56·0 microgrammes per 100 millilitres after seven months and 18·9 microgrammes per 100 millilitres after twelve months following lipiodol administration in one case; in another case, after intravenous pyelography we found 49·1 microgrammes per 100 millilitres after a fortnight, 15·0 microgrammes after three and a half weeks, and still 19·6 microgrammes per 100 millilitres after seven weeks; and in a second case after intravenous pyelography 90·0 microgrammes per 100 millilitres after one week.

Even the thiouracil action did not wear off sometimes for several weeks. The same comment could be applied to thyroid preparations. Recommendations for the length of the medication-free period for different preparations are given in more detail in the paper by Madigan and King (1954).

Discussion.

PBI estimation as a diagnostic aid has been used for several years by overseas workers, and most investigators regard it as a valuable index of thyroid function. In this investigation, as in most others reported, its accuracy has been judged, for lack of a better criterion, by reference to clinical assessment.

It has been stressed repeatedly by Means (1950) and others that various tests used for diagnostic purposes in thyroid disease are not all located in the same area of physiological disturbance. The radioactive iodine uptake studies express the degree of the gland's avidity for iodine; PBI^{131} is dependent on the conversion of inorganic iodide to hormonal iodine and the rate of its release into the blood-stream; the PBI value is the titre of hormonal iodine in the blood at any given time, while the basal metabolic rate is the result of the impact of thyroid hormone on the tissues.

The clinical picture presented by the patient is the composite effect of all these factors. As many other influences are also at work, and the nervous system of the patient is often under severe emotional stress, the symptoms presented on examination can be most variable. In view of this the result of no single laboratory test should be judged on clinical grounds alone, but its usefulness should be assessed by comparison with other well-known procedures.

According to Riggs (1952) the clinician is not interested in the activity of the thyroid gland *per se*, but rather in the action of the thyroid hormone. Hence the ideal diagnostic test according to this author would measure some metabolic effect specifically produced by the hormone in the tissues. Unfortunately no such test is available. While the basal metabolic rate is undoubtedly determined in part by the action of the thyroid hormone, it is also influenced by a wide variety of other factors which are difficult to appraise and impossible to express mathematically. After careful study Riggs comes to the conclusion that the diagnostic test has to be a measure of the rate of secretion of the thyroid hormone, and he assumes that in the absence of interfering medication the concentration of iodine bound to plasma proteins may be taken as a measure of the concentration of the hormone in the extrathyroidal compartment. This has also been confirmed by Chaikoff *et alii* (1947), by Taurog and Chaikoff (1948) and by Rosenberg (1950).

Furthermore, the practical clinical value of any test depends not upon specificity alone, but also upon the simplicity and accuracy of the method used. Above all it depends upon the ability of the test to discriminate between euthyroidism and minimal hyperthyroidism or hypothyroidism.

In view of our experience in this laboratory, we are of the opinion that although the technique used by us does not fulfil Riggs's condition of simplicity, its specificity and accuracy are highly commendable. Amounts of iodine as low as 0·3 microgramme per 100 millilitres encountered in a case of Sheehan's disease (post-partum pituitary necrosis) were easily picked up, and in a series of estimations on two consecutive days PBI values were almost identical. The successive PBI values were 0·3, 0·3, 0·6—average 0·4 microgramme per 100 millilitres—and 0·2 and 0·3—average 0·3 microgramme per 100 millilitres.

Most investigators, in spite of the use of various techniques, claim good over-all agreement between PBI values and clinical diagnosis on large groups of normal euthyroid, hyperthyroid and hypothyroid subjects — Salter *et alii* (1941), 98% (110 cases); Riggs (1947), 85% to 89% (325 cases); Winkler (1947), 90% (397 cases); Connor *et alii* (1949), 90% (887 cases); Starr *et alii* (1950), 74% to 94% (358 cases); Halliman *et alii* (1951), 95% (1446 cases). De Mowbray and Tickner (1952), on the other hand, had only 77% agreement (505 cases). (The percentage of cases in some instances was calculated from the figures given.) All the investigators, of course, had some results which were failures from the clinical point of view, and some "overlap zones" between normal and abnormal limits.

We have obtained an over-all 90% agreement with clinical data (see Figure I), and, in view of our patients being largely in the "clinically borderline" group, we regard our results as very encouraging. Our failures are mostly due to residual effects of various medications (apart from the formerly mentioned case of probable "end organ insensitivity"), although we found that some discrepancies exist between PBI results and clinical symptoms following an I^{131} therapy dose. We intend to clarify this point in our future work.

The false values caused by premedication are a serious drawback to the use of the PBI estimation as the only diagnostic aid and necessitate a very careful and detailed case history and often repeated analyses. These disadvantages, however, apply also to other techniques in use. Radioactive iodine uptakes are almost equally sensitive to iodine or thyroid intake, while any excretion indices depend on unimpaired renal function and complete collection of the specimen. Whether the radioactive iodine indices are affected by contrast media used for X-ray techniques has not been conclusively proved. Forty-eight hour PBI^{131} estimation is under investigation in the Commonwealth X-Ray Laboratories and will be discussed in a paper to be published shortly (Clarke and Aujard, 1954).

The only logical conclusion is the simultaneous use of several indices derived from the use of several different techniques concerning various aspects of thyroid activity. The choice is wide. Means recommends the use of the "triad"—forty-eight hour radioactive iodine uptake, PBI value and basal metabolic rate (see Tables I and II), while Riggs advocates the combination of radioactive iodine studies with PBI in blood and iodine in urine. Other workers have used various other combinations of indices to good advantage.

Statistical analysis on a group of results in Melbourne in which PBI estimation is combined with several physical indices favours the joined results of k_1 (I^{131} uptake rate) and PBI value expressed by the following mathematical formula:

$$\text{Criterion} = 1{\cdot}909 \sqrt{\text{PBI}}\ \mu\text{g. per 100 mls.} + 2{\cdot}297 \log k_1 - 4{\cdot}838$$

If this criterion was adopted, then all patients giving positive results would be considered in a toxic state, all giving negative results would be considered in a non-toxic state. There would be a 6% misclassification.

In conclusion, in view of the delicate laboratory technique, we cannot recommend PBI estimation as a standard hospital procedure. Even the simplified methods appearing in the literature with which we are not experienced require well-trained staff and a room set apart for iodine estimations. In our opinion it would be better to set up a suitable central iodine assay laboratory in every State. This laboratory could supply physicians with appropriately treated glassware for blood collection and give all necessary instructions to avoid any factors likely to invalidate the test. The simple dispatch of a blood sample would not put an undue burden on a busy physician even in a remote country area.

Summary.

1. The PBI fraction has been estimated in the plasma of 106 normal individuals and of 137 patients suspected of

having thyroid disease. The results include 294 PBI values each of which is a mean of from one to three analyses (in duplicate) on day-to-day samples. Most of the estimations were made concurrently with I^{131} tracer studies, and all of them are compared with clinical assessment.

2. The normal range (confirmed by a statistical analysis carried out on a sufficient number of cases) was from 2·7 to 8·0 microgrammes per 100 millilitres for 95% and 3·0 to 7·5 microgrammes per 100 millilitres for 90·5% of normal population; 2·7 to 3·0 microgrammes per 100 millilitres and 7·5 to 8·0 microgrammes per 100 millilitres are regarded as borderline zones where the normal and abnormal values overlap.

3. In the group of 106 normal controls, 101 or 95% PBI values were within the normal range. Out of these, four were in borderline zones. The mean value was 5·16 microgrammes per 100 millilitres.

4. In a group of 70 patients with various diseases, but clinically diagnosed as euthyroid, 83 tests (91%) out of 92 gave PBI values between 2·8 and 7·7 microgrammes per 100 millilitres. Four were in the borderline ranges. The mean value was 5·2 microgrammes per 100 millilitres (essentially the same as for normal controls). Amongst the misclassified patients of this group were those who had had I^{131} therapy dose or mercurial diuretics a short time before the tests, patients with acromegaly and infective hepatitis, and one with a suspected "end organ insensitivity".

5. In the clinically hyperthyroid group of 40 patients, 64 tests (90%) out of the total 70 gave PBI values as from 7·5 to 20·6 microgrammes per 100 millilitres. Mean was 10·2 microgrammes per 100 millilitres. Out of these, seven were borderline figures. Misclassification occurred after prolonged therapy with antithyroid drugs after I^{131} therapy dose, and in relation to two patients pronounced "slightly toxic" clinically.

6. In the small group of 10 hypothyroid individuals, nine PBI values were from 0·3 to 2·9 microgrammes per 100 millilitres (90%). Two were in the borderline range. The mean was 2·1 microgrammes per 100 millilitres. The misclassified case was the one mentioned in the euthyroid group, in which "end organ insensitivity" was suspected.

7. In the group of 16 tests in which interfering medication was in evidence, PBI values were from 5·2 to 56·5 microgrammes per 100 millilitres for the euthyroid and from 1·5 to 28·0 microgrammes per 100 millilitres for the hyperthyroid section.

8. For the accuracy of the test we regard it as important (*a*) to observe the various precautions as set out in the text, (*b*) to perform two or three PBI tests on day-to-day samples and regard the mean value as the correct figure.

9. In view of the large percentage of difficult and borderline cases amongst our patients, we regard the low percentage of misclassifications as a proof that the PBI estimation is a valuable aid to diagnosis in thyroid dysfunction.

10. The benefit of using tests covering different aspects of thyroid function is briefly discussed.

Acknowledgements.

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References.

BARKER, S. B. (1948): "Determination of Protein Bound Iodine", *J. Biol. Chem.*, 173: 715.

CHAIKOFF, I. L., TAUROG, A., and REINHARDT, W. O. (1947), "The Metabolic Significance of Protein-bound Iodine in Plasma: A Study of its Concentration under Various Conditions and of its Rate of Formation as Measured with Radioactive Iodine", *Endocrinology*, 40: 47.

CLARKE, K. H., and AUJARD, R. L. (1954), "The Use of Radio-Active Iodine (I^{131}) in the Diagnosis of Hyperthyroidism (Physical Aspects)", M. J. AUSTRALIA, in the press.

CONNOR, A. C., CURTIS, G. M., and SWENSON, R. E. (1949), "A Simplified Method for the Determination of the Protein Bound Iodine and its Clinical Application", *J. Clin. Endocrinol.*, 9: 1185.

DANOWSKI, T. S., HEIDENBERG, S., and GREENMAN, J. H. (1949), "The Constancy of the Serum Precipitable Iodine or PBI in Healthy Adults", *J. Clin. Endocrinol.*, 9: 768.

DANOWSKI, T. S., *et alii* (1950), "Serum Iodine Fractions in Subjects Receiving Potassium Iodide in Small Doses", *J. Clin. Endocrinol.*, 10: 532.

DANOWSKI, T. S., JOHNSTON, S. Y., and GREENMAN, J. H. (1950), "Alterations in Serum Iodine Fractions Induced by the Administration of Inorganic Iodide in Massive Doses", *J. Clin. Endocrinol.*, 10: 519.

DANOWSKI, T. S., *et alii* (1952), "Serum PBI during Ingestion of Desiccated Thyroid", *J. Clin. Endocrinol.*, 12: 1572.

ENGSTROM, W. W., *et alii* (1950), "Effect of Thiourea and Iodine on SPI", *J. Clin. Endocrinol.*, 10: 1251.

FERTMAN, M. B., and CURTIS, C. M. (1951), "Food and the Genesis of Goiter", *J. Clin. Endocrinol.*, 11: 1361.

FREDRICKSON, D. S., FORSHAM, P. H., and THORN, G. W. (1952), "The Effect of Massive Cortisone Therapy on Measurement of Thyroid Function", *J. Clin. Endocrinol.*, 12: 541.

GROSS, J., and PITT-RIVERS, R. (1952), "The Identification of 3:5:3'-L-triiodothyronine in Human Plasma", *Lancet*, 1: 439.

GROSS, J., and PITT-RIVERS, R. (1953), "3:5:3'-L-Triiodothyronine. 2. Physiological Activity", *Biochem. J.*, 53: 652.

HALLMAN, B. L., BONDY, P. K., and HAGEWOOD, M. A. (1951), "Determination of Serum Protein-bound Iodine as a Routine Clinical Procedure", *Arch. Int. Med.*, 87: 817.

HEINEMAN, M., JOHNSON, C. E., and MAN, E. B. (1948), "Serum Precipitable Iodine during Pregnancy", *J. Clin. Investigation*, 27: 91.

HYDE, L. R., and HYDE, B. (1949), "Effect of Retained Bronchial Lipiodol on Blood Iodine", *J. Lab. & Clin. Med.*, 34: 1516.

KYDD, D. M., and MAN, E. B. (1951), "Precipitable Iodine of Serum in Disorders of the Liver", *J. Clin. Investigation*, 30: 874.

KYDD, D. M., MAN, E. B., and PETERS, G. P. (1950), "The Concentration of Precipitable Iodine in the Serum", *J. Clin. Investigation*, 29: 1033.

MADIGAN, J. P., and KING, W. E. (1954), "Radio-Active Iodine (I^{131}) and Protein-Bound Iodine in Thyroid Disorders", M. J. AUSTRALIA, 1: 801.

MAN, E. B., and PETERS, G. P. (1950), "Artifactual Values of Serum Precipitable Iodine", *J. Lab. & Clin. Med.*, 35: 280.

MAN, E. B., *et alii* (1951), "The Precipitable Iodine of Serum in Normal Pregnancy and its Relation to Abortions", *J. Clin. Investigation*, 30: 137.

MAN, B. E., KYDD, D. M., and PETERS, J. P. (1951), "Butanol Extractable Iodine of Serum", *J. Clin. Investigation*, 30: 531.

MEANS, J. H. (1950), "Comparison of Tests of Thyroid Function", *Bull. New York Acad. Med.*, 26: 583.

DE MOWBRAY, R. R., and TICKNER, A. (1952), "The Diagnostic Value of Estimations of Protein-bound Iodine in Serum", *Lancet*, 2: 511.

MEYERS, J. H., MAN, E. B., and CONN, J. W. (1951), "Artifactual Values of Serum Precipitable Iodine after Clinical Intramuscular Injections of Mercurihydrin", *J. Lab. & Clin. Med.*, 37: 867.

PERLMUTTER, M., and RIGGS, D. S. (1949), "Thyroid Collection of Radioactive Iodide and Serum Protein Bound Iodine Concentration in Senescence in Hypothyroidism and in Hypopituitarism", *J. Clin. Endocrinol.*, 9: 430.

RAPPORT, R. L., and CURTIS, G. M. (1950), "The Chemical Significance of Blood Iodine: A Review", *J. Clin. Endocrinol.*, 10: 735.

RIGGS, D. S., and MAN, E. B. (1940), "A Permanganate Acid Ashing Micromethod for Iodine Determinations; Values in the Blood of Normal Subjects", *J. Biol. Chem.*, 134: 193.

RIGGS, D. S. (1947), "Serum Protein Bound Iodine as a Diagnostic Aid", *Tr. Am. A. Study Goiter*, 137.

RIGGS, D. S. (1952), "Quantitative Aspects of Iodine Metabolism in Man", *Pharmacol. Rev.*, 4: 284.

ROSENBERG, I. N. (1951), "The Nature of the Circulating Thyroid Hormone in Graves's Disease", *J. Clin. Investigation*, 30: 1.

SALTER, W. T., BASSETT, A. M., and SAPPINGTON, T. S. (1941), "Protein Bound Iodine in Blood", *Am. J. M. Sc.*, 202: 527.

STARR, P., *et alii* (1950), "Clinical Experience with Blood Protein Bound Iodine Determination as a Routine Clinical Procedure", *J. Clin. Endocrinol.*, 10: 1237.

TAUROG, A., and CHAIKOFF, I. L. (1948), "The Nature of the Circulating Thyroid Hormone", *J. Biol. Chem.*, 176: 639.

TUCKER, R. G., and KEYS, A. (1951), "Concentration of Serum PBI in Normal Men", *J. Clin. Investigation*, 30: 869.

WILLIAMS, R. H. (1948), "Relation of Obesity to the Function of the Thyroid Gland Especially as Indicated by the Protein Bound Iodine Concentration in the Blood", *J. Clin. Endocrinol.*, 8: 257.

WINKLER, A. W. (1947), Quoted by SKANSE, B. (1949), in "Radioactive Iodine in the Diagnosis of Thyroid Disease", *Acta med. scandinav.*, Supplement 235.

ZAK, B., KOBN, A., and BOYLE, A. J. (1953), "Normal and Abnormal Values of Protein-bound Iodine", *Am. J. Clin. Path.*, 23: 603.

Reports of Cases.

RUPTURED PEPTIC ULCER OR DIABETES MELLITUS?

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As the title of this paper would suggest, the following case presents some unusual aspects in differential diagnosis. There are, of course, many conditions simulating ruptured peptic ulcer which must be differentiated before operation is performed, but *diabetes mellitus* is not usually one of them in the early stages.

Clinical Record.

Mr. X., aged thirty-nine years, presented as a new patient on October 3, 1952, with severe generalized abdominal pain of two or three hours' duration. The onset had been sudden, one or two hours after breakfast, with only general malaise as a premonitory warning before and at that mealtime. The pain was maximal in the upper half of the abdomen. There was pronounced nausea, and some vomiting had occurred at the onset. There was no history of a previous attack or of any past indigestion. He had indulged excessively in alcohol on the previous night.

On examination, the patient was lying supine in obvious severe distress, breathing was rapid and shallow, and he appeared pale and clammy, and was gasping to those nearby to "do something". His temperature, pulse rate and blood pressure were all normal. No other abnormality was revealed except in the abdomen, which was immobile and tender, especially in the epigastrium. This rigidity was almost classically board-like and was certainly not voluntary on the part of the patient. There was no diminution of liver dullness, and a rectal examination revealed no abnormality. A specimen of urine could not be obtained at the time.

He was admitted to the Woomera Hospital with the diagnosis of suspected perforated peptic ulcer; a plain X-ray film of the abdomen, with the patient in the upright and supine positions, revealed no gas under the diaphragm, and an X-ray film of the chest revealed no abnormality. The patient was prepared for laparotomy, intravenous therapy and gastric suction were instituted, and the administration of the anæsthetic had almost commenced when a report of the urine test came to hand; the urine was acid, its specific gravity was 1·028 and it contained a large amount of sugar and a trace of acetone. A rather critical problem thus arose. Was he a diabetic with a coincidental ruptured ulcer (the age-old fallacy of diagnosing two conditions in the one patient); was he a diabetic only (very unusual); or had he a ruptured ulcer and glycosuria from causes other than diabetes (very unlikely)? What a triad!

As neither the other medical officer nor myself was acquainted with any such condition solely attributable to *diabetes mellitus*, it was decided not to risk conservative treatment and laparotomy was performed. The reader may have guessed the result—no abnormality was found. This was a little disappointing, but nevertheless we were comforted in a negative way by the fact that we were not "sitting" on a ruptured ulcer.

Convalescence was uneventful, and the patient's condition was stabilized on a liberal diet with 25 units of protamine zinc insulin daily. Later a glucose tolerance test revealed a typical diabetic curve.

This account is not complete without the recording of a rather interesting event which occurred four months later; during this time another medical officer had replaced my previous partner.

Once more Mr. X. presented to me with precisely the same symptoms, and I learnt that he had not continued with his insulin for some weeks, having relied only on his diet; added to this, he had been consuming alcohol in excess for the last few days.

My colleague examined the patient, armed only with the knowledge that the abdominal scar was the result of a laparotomy for a suspected peptic ulcer four months previously, and his diagnosis, without his knowing the result of the urine test, was a recurrence of the ruptured ulcer. However, the "ruptured ulcer" was this time "cured" by the simple expedient of administering 50 units of soluble insulin and 50 grammes of glucose, repeated as indicated by the results of the urine tests, although one-quarter grain of morphine was also required initially.

His condition was again stabilized, but this time 25 units of protamine zinc insulin and 25 units of soluble insulin were required.

Discussion.

The extent to which this strange and unusual attack of abdominal pain in *diabetes mellitus* simulated a ruptured peptic ulcer is revealed by the unanimous diagnosis formulated by three practitioners after separate examinations.

Abdominal pain in severe hyperglycæmia, or more correctly ketosis, is well known; but pain of the severity described above, together with the extreme rigidity and tenderness, must be uncommon.

An interesting question obviously arises—namely, what was the origin of this severe pain and tenderness? I am at a loss to produce a satisfactory answer, and any comments on this case, and in particular reports of any similar cases would be welcomed.

Reviews.

Official History of the Canadian Medical Services, 1939-1945; Volume II: Clinical Subjects, edited by W. R. Feasby, B.A., M.D.; 1953. Published by authority of the Minister of National Defence. Ottawa: Edmond Cloutier, C.M.G., O.A., D.S.P., Queen's Printer and Controller of Stationery. 10" × 6¼", pp. 556, with 16 illustrations; five in colour. Price: $5.00.

IN his preface, Colonel Feasby has clearly indicated his intention of confining the contents of this publication to a concise record of the Canadian Medical Corps in all three Services, referring briefly only to many of the activities and in more detail to matters of importance or outstanding work. He has included in full detail the very valuable statistics without which no account such as this can be complete.

This obviously was a task of considerable magnitude, embracing as it did the collection of all the relevant information from the Navy, Army and Air Force. Colonel Feasby acknowledges assistance from selected sources and individual contributions, but the main burden of collation, publication and indeed of personal contribution has been his responsibility. He has achieved an outstanding success along the preconceived lines on which the history was planned and deserves praise for having effectively combined interest with requisite information.

War of any magnitude provides remarkable opportunities and inducement for medical research. It is perhaps a matter for regret that more space has not been devoted to the descriptions of the research investigations undertaken by the Canadian Medical Services. The development in the organization and work of various consultants within the Navy, Army and Air Force is another aspect of great importance. Here, too, more elaboration might well have enhanced the value to posterity of this publication as a book of reference.

The chapter on neurology and psychiatry is profoundly interesting. In company with all countries engaged in total war, Canada was beset with psychiatric and psychological problems affecting its Services and the civilian population. The importance of these has been stressed admirably and their far-reaching nature described. Of particular interest is the part dealing with the management and care of psychological casualties in the field. The reader cannot fail to be impressed with an organization that recognized both the necessity for special treatment or care and the importance of providing special units to which such of these subjects could be sent as were unfit for front line service but were in other respects capable of employment. The Special Employment Companies and the Corps Exhaustion Unit played an important part in attempting to deal with this problem. As

the author states: "The only cases requiring evacuation from the theatre of war were the psychotic and prepsychotic group and the occasional patient suffering hysterical or terror states who could not achieve calm until England was reached."

Another problem of total war was the adequate use of all suitable personnel, especially with the idea of conserving man power. This called for the closest scrutiny of all available resources by individual countries, and in Canada led to the introduction of the Pulhems system as a method of designating mental and physical fitness. This was found to give excellent results and has been justifiably described in some detail. The success obtained was so outstanding that it has been adopted by the armed forces of many other countries including the United Kingdom.

The statistical tables are excellent and most complete and, while of considerable interest even to the casual reader, provide extremely valuable records. Their careful compilation and wide embracing nature make them an outstanding feature of this volume.

The scope of this volume is considerable. The author is to be congratulated on his successful handling of so vast an amount of material, for, while he has indicated the widespread nature and activities of the Canadian Medical Services, he has confined himself to essentials with modest emphasis on achievements and has produced a book that is full of interest, not only for the ordinary medical reader, but for the student of military medical history in its application to the general and special problems peculiar to war.

This review would not be complete without enthusiastic reference to the illustrations and photographs, which are preeminently good. Here, too, the only note of regret is that more of them could not have been included in the book. The reproductions of both paintings and photographs alike are first rate. The format, printing and general arrangement of the book leave nothing to be desired. Much praise is due to the Canadian Department of Defence for the actual publishing.

Atomic Medicine. Edited by Charles F. Behrens, M.D.; Second Edition; 1953. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 9" × 6¼", pp. 646, with 130 illustrations. Price: £5 18s. 3d.

THE rapid developments in the production of atomic energy, and the increasing application of high energy radiations and radioisotopes in medicine have led to the appearance within four years of a second edition of this book. Many of the earlier chapters have been considerably amplified in the light of more recent knowledge, and new sections dealing with the administration and dosimetry of radioisotopes, and with protection against radiation and defence against atomic weapons have been included. The entire volume has been increased from 416 to 632 pages.

The book contains 22 chapters, each written as an essay by a contributor with special interest in the subject. The majority of the contributors are members of the United States Navy Medical Corps. Since many of the subjects are interrelated, there is a certain amount of overlapping of material, but this is not a serious disadvantage to the reader.

The early chapters deal with the fundamental physics of atomic structure and radioactivity, the various types of ionizing radiations, and the production and general effects of atomic bombs. One chapter deals in general terms with the development of high-voltage generators for the production of radiation with energies up to tens of millions of volts. The biological, pathological and hæmatological effects of radiation are then discussed in some detail. Methods of detecting and measuring radiation and of protecting personnel are described. Civil defence procedures against atomic bombs are discussed somewhat briefly.

The greatest additions from the first edition occur in the later chapters. These deal with the use of radioisotopes as tracers in physiological investigations, and in the diagnosis and treatment of diseases. Information is given on the design and operation of a laboratory in which radioisotopes are used, and on the methods of administration and estimation of dosage. The effects of radiation on the teeth and jaws is discussed briefly. The book concludes with a number of appendices showing various types of radioisotopes and their physical characteristics, as well as definitions of terms.

It is inevitable that one volume attempting to cover such a range of topics will not satisfy all types of readers. Medical workers wishing to learn something of the effect of atomic developments on medicine will find much of interest, and bibliographies given at the end of each chapter will provide a starting point for further reading. The specialist, however, who has, for example, had some experience in the use of radio-phosphorus and radio-iodine, may well be somewhat disappointed. In particular, the bibliographies on these two subjects do not include quite important recent papers by English and European workers. The radiologist, too, may question the value of the short reference to the linear accelerator on page 342, which does not mention the progress made in England with this type of high tension generator.

The general reader may also puzzle over some of the diagrams. In some cases the diagram is not referred to in the text; in others, the point which was to be illustrated does not appear to be well made.

Notwithstanding these criticisms, the second edition of this book should find a place in all medical reference libraries.

The Vitamins in Medicine. By Franklin Bicknell, D.M., M.R.C.P., and Frederick Prescott, M.Sc., Ph.D., F.R.I.C., M.R.C.P.; Third Edition; 1953. London: William Heinemann (Medical Books); Limited. 10" × 6¼", pp. 792, with 242 illustrations. Price: 70s.

THE first (1942) and the second (1946) editions of this book by Franklin Bicknell and Frederick Prescott were reviewed favourably in these columns, and the opinion was expressed that the book would be regarded as the standard work of reference on the subject. Now a third enlarged and revised edition has been published bringing the subject more up to date and covering the enormous mass of literature on this nutritional and medical topic. There are now over 5000 references and this assuredly represents laborious scholarship, for the text proves that this is not mere card-indexing, but that each paper has been read and assimilated. The general plan of the book remains the same; each vitamin from *A* to *P* is considered under the headings history, chemistry, sources, physiology, pharmacology, human requirements, deficiency diseases, methods used for detecting deficiencies and clinical applications. The illustrations, mostly excellent, have been increased from 208 to 245. The least satisfactory chapter is that on vitamin *E*, but this arises from paucity of human material and is not the fault of the authors, who admit that "vitamin *E* has been considered to be of no importance in human nutrition". This admission is followed by the sarcastic comment: "But it is fantastic to believe that while mice and monkeys, ducks and dogs, beetles and barrows all need vitamin *E*, yet a beneficent all wise providence has excused man from this irksome necessity."

It is certainly curious that when nutritional writers take up the subject of white bread they lose the philosophical calm which a scientific exposition should display. We have not in Australia personal experience of the regulations to which the authors object, but such an expression as "the Government in its infinite lunacy" carries no conviction; an uncoloured statement of fact would, we venture to think, be more effective. Apart from this trivial matter the presentation is clear and convincing, and the book may now be considered as an indispensable addition to the library not only of the nutritional expert but of the medical practitioner.

Pediatric Gynecology: With Sections on Urology and Proctology. By Goodrich C. Shauffler, M.D.; Third Edition; 1953. Chicago: The Year Book Publishers, Incorporated. 9" × 6¼", pp. 318, with 76 illustrations. Price: $7.50.

THIS book was first published in 1942 and is now in its third edition, which is a complete revision and includes an extra chapter on the embryological development of the female genital system.

Dr. Schauffler has obtained the assistance of a series of specialists for the chapters on certain non-gynæcological but related subjects such as general surgical considerations, urological and proctological considerations, social service and medico-legal aspects.

Though the scientific and sociological information is doubtless of the most recent nature, the general philosophy of the advisory matter is sanely conservative. Mischievous and meddlesome surgery such as clitoridectomy for masturbation or for any other reason short of malignant disease is firmly and positively interdicted. Female circumcision should be a rarity, though probe dissection of preputial adhesions is advocated when clearly indicated.

In the absence of sufficient factual and proven knowledge concerning precipitation of the menarche and liability to pregnancy for two or three years thereafter even where child marriage is practised the author is obliged to be conventional, but deprecates the persisting prominence of unenlightened matriarchal folklore and prudish taboo. Positive planned instruction on matters of sex is not advocated, but should be conveyed from doctor to patient without inhibition as the occasion arises. Moreover, the attending

doctor should not neglect careful examination of the genitalia on appropriate occasions for the elucidation of a physical basis for significant symptoms. In a general way, theoretical concepts such as the Freudian psychological hypotheses have not been found useful for solving juvenile problems.

The auxiliary chapters to which reference has already been made enhance considerably the interest and usefulness of the book. It is not difficult to translate the social and medico-legal facts from their American environment into our own field as the general principles and broad outlines coincide. As is usually the case, the American scene seems to be more variegated and mature than the Australian one; our neighbours have gone further and have spent much time, money and human energy on sociology. They have stimulated others to profit by their successes and their mistakes and to forge ahead to raise the standards of social activities in democratic communities. The stage they have reached in the field of pædiatric gynæcology (using the term in its broadest sense) is described well in this particularly interesting and informative book.

Cortisone and ACTH: In Clinical Practice. Edited by W. S. C. Copeman, O.B.E., M.D., F.R.C.P., with a foreword by The Lord Horder, G.C.V.O., M.D., F.R.C.P.; 1953. London: Butterworth and Company (Publishers) Limited. Sydney: Butterworth and Company (Australia), Limited. 9" × 6", pp. 266, with 29 illustrations. Price: £1 15s. 6d.

SINCE the announcement in 1949 by Hench and his colleagues of the first trials of cortisone and ACTH in the treatment of rheumatoid arthritis and rheumatic fever, the contributions to the world literature on all aspects of the use of these hormones have been so great that it has been difficult to keep abreast of the progress of knowledge. While much of the work done has been in the United States of America, where supplies have been more plentiful, many careful trials have been made in Great Britain. This book combines the personal experience of seven authors with a review of the relevant literature up to 1952. One senses the typically cautious British approach to a new therapeutic weapon. The present position of these hormones in therapy is set out clearly and the precautions necessary in their use are stated concisely. The relevant experimental data, illustrative case histories and where appropriate, diagrams and illustrations are given so that the reader gets a balanced view of the practical management of the various diseases in which cortisone and ACTH are of use.

There are six chapters, the first of which, by Oswald Savage and W. S. C. Copeman on rheumatic and collagen diseases, is the longest. In this chapter is a review of the history, chemistry, physiology and general therapeutic effects of the hormones. The suggestions for the management of rheumatic and collagen diseases correspond closely with the experience of some Australian practitioners and may be used confidently by readers of the book. There is some overlapping in the presentation by the authors of the various chapters, as may be expected from separate contributors. No inconsistencies have been observed. Chapters are devoted to diseases of the eye, endocrine disorders, respiratory and allergic diseases, skin diseases and diseases of the hæmatopoietic system.

In view of the potentialities of these hormones in altering the morbidity of many diseases, and the mortality of some, all practitioners must keep up to date on the indications and contraindications for their use. This book is a concise and accurate source of this knowledge.

The Normal Child: Some Problems of the First Three Years and Their Treatment. By Ronald S. Illingworth, M.D. (Leeds), F.R.C.P. (London), D.P.H., D.C.H.; 1953. London: J. and A. Churchill, Limited. 9¼" × 6¼", pp. 352, with 64 illustrations. Price 30s.

THE sub-title of this book indicates and delimits the contents. Considerable emphasis is placed on the importance of the inclusion in pædiatrics of a systematic study of all that pertains to children and to normal childhood.

The four sections of the book are devoted respectively to feeding problems, physical problems, developmental problems and behaviour problems.

In the first section Professor Illingworth discusses in telling fashion the overwhelming advantages of natural over artificial feeding in early infancy. He expresses a preference for a self-demand schedule instead of the tyranny of the clock and is satisfied that faulty habits are not inculcated thereby though some mothers find a rigid routine easier to follow. In a friendly lucid and authoritative manner the usual feeding problems are described, and sound advice is proffered for overcoming them.

The Wetzel grid for babies is reproduced in the second section, and the statement occurs that, in general, serial weight and height records provide the most useful information about a child's growth. Due allowances must be made for factors other than disease known to affect growth. The size and shape of the skull, the teeth, the skin and umbilicus, the breast and genitals and some miscellaneous problems of a physical nature are traversed, and the section ends with a good chapter on the prevention of infection.

The normal course of development and the general and special factors which affect it are summarized competently in the third section which is an unusually valuable background for the important final one.

Professor Illingworth's outstanding contribution is the discussion of the common behaviour problems of babies and toddlers; this is covered in about one hundred pages of potted wisdom which should be distributed widely beyond the confines of the medical profession.

The book is attractively produced and its contents are so valuable and so well presented that it should be assured of a welcome and a wide distribution.

Books Received.

[*The mention of a book in this column does not imply that no review will appear in a subsequent issue.*]

"Chemotherapy of Infections", by H. O. J. Collier, B.A., Ph.D., M.I.Biol., with a foreword by Alexander Fleming; 1954. London: Chapman and Hall Limited. 7½" × 6", pp. 264, with 53 illustrations. Price: 18s.

One of the "Frontiers of Science Series" published under the general editorship of Dr. Bernard Lovell.

"Embolia y Trombosis", by Th. Naegeli and P. Matis; 1954. Barcelona: Folia Clinica Internacional. 9" × 6½", pp. 162, with 12 text-figures.

A comprehensive monograph on embolism and thrombosis, which the authors regard as different aspects of the one condition of thrombo-embolism. The monograph is based on a review of the world literature of the subject as well as on the authors' extensive experience. It is written entirely in Spanish.

"Clinical Medicine: Some Principles of Thinking, Learning and Teaching", by R. D. Lawrence, M.A., M.D. (Aberdeen), F.R.C.P.; 1954. London: H. K. Lewis and Company. 9" × 6", pp. 72. Price: 7s. 6d.

The author presents some principles which he has found helpful in minimizing his own errors.

"Guide to the Classification and Identification of the Actinomycetes and their Antibiotics", by Selman A. Waksman and Hubert A. Lechevalier; 1953. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson Limited. 9" × 6", pp. 254. Price: 53s. 9d.

The title of the book describes its scope and purpose.

"Plague", by R. Pollitzer, M.D.; 1954. Geneva: World Health Organization. 9½" × 6½", pp. 698, with 40 illustrations, one in colour. Price: £3 5s. (cloth-bound), £3 (paper-bound).

Deals with every aspect of the subject, including history and prophylaxis.

"Modern Trends in Diseases of the Ear, Nose and Throat", edited by Maxwell Ellis, M.D., M.S., F.R.C.S.; 1954. London: Butterworth and Company (Publishers) Limited; Sydney: Butterworth and Company (Australia) Limited. 10" × 7", pp. 480, with 140 illustrations. Price: 90s.

One of the well-known "Modern Trends" series which is under the general editorship of Lord Horder.

"Modern Trends in Dermatology (Second Series)", edited by R. M. B. McKenna, M.A., M.D. (Camb.), F.R.C.P. (London); 1954. London: Butterworth and Company (Publishers) Limited; Sydney: Butterworth and Company (Australia) Limited. 10" × 7", pp. 348, with 58 illustrations. Price: 86s. 6d.

The first edition was published in 1948.

The Medical Journal of Australia

SATURDAY, JUNE 5, 1954.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

OLFACTORY PATHOLOGY.

If it is true that there is no proper pathology which is not built upon a solid substratum of physiology, then the pathology of smell is in a parlous state. Actually pathological conditions have met with more success in description and classification than the purely physiological. The actions of trauma, such as cranial fracture, or degenerative changes in the nasal membranes in producing abolition or reduction of olfactory perception are well known, but despite much experimentation the physiological basis remains a mystery. Man has been described as microsmatic, that is, possessing a poorly developed sense of smell as compared with most mammals, and in this can be classified with rats and other rodents, monotremes and cetaceæ. The usual explanation of the low acuity of smell in man is that the hands, which the erect posture has shielded from use in support and progression and which are placed at the exclusive direction of the brain, must be guided by vision; further, the elevation of the head above the ground has helped in the removal from the olfactory sphere of action of the distance-perception of quarry, enemy, stranger and sex mate. Degenerate as the human sense of smell is when compared with that of dog, pig, horse and most insects, we still are faced with a discriminative delicacy which transcends the most refined methods of spectral analysis. Valentin calculated that even $^{3}/_{100000000}$ grain of musk can be detected. One milligramme of skatol would make a hall 500 metres long, 100 metres wide and 50 metres high very unpleasant. This of course is not to be compared with the female gypsy moth, which can attract the male at two miles and more distance through an odorous emanation. Even the female dog in œstrus can arouse interest in males a long way off. Still the acuity we possess is surprisingly great, and as yet suggested chemical and physiological mechanisms have thrown but little light on the problem. Attempts to correlate odour with chemical constitution have failed sadly; substances closely allied in structural formula have widely different odours, and several sets of compounds can be named with precisely similar odours but without any chemical affinity whatsoever. At one time some help was expected from immunity postulates in that each odorous body was supposed to contain a haptophore or anchoring attachment and an osmaphore or group responsible for the excitation of the olfactory receptors, but the hopes centred on this hypothesis turned out to be illusory. It has been estimated that the smells which a normal human being can detect and classify number between one thousand and four thousand; and here it may be mentioned that frequently an organic substance new to chemistry has been synthesized possessing a distinctive and unique odour. Recent researches of Professor Adrian, of Cambridge, not yet completed, rather indicate that in the olfactory area there may be two sets of receptors, one basal and primitive like the protopathic sense in the skin or the rods in the retina, the other epicritic giving fine discriminative analysis. In smell as in taste there is often a contribution from the fifth nerve. A jelly which has set may be pleasant; the same jelly before it has set is mawkish; and yet the two are chemically identical. This fragmentation in the mouth, of which we are cognizant through the fifth nerve, is responsible for much of the pleasure in eating celery, biscuits and many fruits. Also in the nose varying velocity of air currents and alterations of temperature and humidity in the inspired air may reinforce purely olfactory sensations.

A most interesting field of research, as yet untraversed, is the possible relation of vitamin *A* to the sense of smell. In the work, which may without exaggeration be called authoritative, on vitamins in medicine, by Franklin Bicknell and Frederick Prescott (third edition, 1953) there occurs the following statement regarding vitamin *A* deficiency:

> Loss of smell is a late but constant finding in rats and other mammals, though the olfactory epithelium appears to be normal. The olfactory nerve endings themselves may be damaged by osseous thickening of the cribriform plate. Milas found that the olfactory area in the steer was rich in carotenoids and vitamins A_1 and A_2, which suggests that vitamin *A* may play a part in smell analogous to that it plays in vision. It would be interesting to know if a deficiency of vitamin *A* in man causes loss of smell.

Now the relation of vitamin *A* to visual purple is known and the results of deficiency are easily explained, but the problem is not so simple in olfactory perception. To find examples of vitamin *A* deficiency in food one would have to visit and examine certain primitive races and communities, for such a dietary condition is hardly likely to be found in civilized countries; but there is one pathological condition in which deficiency of vitamin *A* may easily be present, and that is in inflammatory affections of the liver. It is in the liver that vitamin *A* is accumulated for future use. The liver of the polar bear and seal, which the Eskimos refuse to eat and which dogs and carnivorous birds avoid, can produce acute poisoning when consumed by Arctic explorers, and this through excess of vitamin *A*. When the liver is inflamed or in any way reduced in activity some interference with the storage

and distribution of vitamin *A* is inevitable, and it is just here that research may reveal some interesting facts. Already there is a little evidence that one of the sequelæ of infectious hepatitis is reduction in olfactory discrimination. This can well be a useful field of investigation, and one which, strange to say, has not yet attracted the attention it deserves.

Current Comment.

ACUTE HÆMORRHAGIC LEUCOENCEPHALITIS.

IN THE MEDICAL JOURNAL OF AUSTRALIA of July 5, 1941, E. Weston Hurst, who was at that time director of the Institute of Medical and Veterinary Science, Adelaide, reported two cases of acute hæmorrhagic leucoencephalitis. This name was given by Hurst to what he maintained was a previously undefined entity. It was "an acute nervous disease, characterized by severe damage to the walls of blood vessels, perivascular necroses, perivascular and focal demyelination, intense polymorphonuclear exudation, and microglial reaction". He pointed out that where lesions were most severe, œdema and hæmorrhages were conspicuous. In the cerebrum the lesions were confined almost exclusively to the white matter. Clinically, the chief feature was a rapid or rather rapid abrogation of the higher cerebral functions in a previously healthy individual; this was associated with headache, vomiting, slight pyrexia or leucocytosis. In 1945 Bruce Shallard and Oliver Latham reported an additional case of the condition in this journal in the issue of February 10. The case, which they described in considerable detail, conformed to those reported by Hurst in 1941.

T. Crawford,[1] of Saint George's Medical School, London, has now reported three cases of the condition, and, as he points out, these bring the reported cases to a total of 10. The object of his communication is to put his three cases on record and also to draw the attention of general pathologists to the existence of this variety of encephalitis. He thinks that the records of the cases published strengthen Hurst's contention that acute hæmorrhagic leucoencephalitis is a specific disease entity distinct from other forms of encephalitis. In a short discussion on the clinical features he points out that the duration of the disease is variable. In seven cases the onset of neurological signs was preceded by a prodromal period of upper respiratory infection lasting from as short a period as two days up to fifteen days. In all cases the prodromal infection was separated from the encephalitic stage by a few days of apparent recovery. The longest survival after the onset of neurological signs was six days; Hurst's original patient died after an illness of only forty-two hours' duration. In regard to the actual lesion, Crawford states that the most characteristic finding consists of hæmorrhages in the white matter of the cerebral hemispheres, varying in size from minute points up to areas a few millimetres in diameter. In the more severely involved regions these hæmorrhages may be confluent. The parts more affected show asymmetrical œdematous swelling with pinkish or grey discoloration. The most severely affected area may have almost a gelatinous consistency. The distribution of the lesions is highly characteristic. The hæmorrhages involve the white matter only, the grey matter showing nothing more than some vascular engorgement. The central white matter of one or both cerebral hemispheres is regularly involved and in most cases has shown the most severe lesions. The hæmorrhages may extend into the white cores of the convolutions, but the U-fibres between the adjacent convolutions are, as a rule, spared. The level to which the lesions descend has varied considerably. It has been noted in the cerebral peduncles in three cases and in the pons in four. In one of Crawford's cases the white matter of the cerebellar hemispheres was involved.

Crawford discusses the ætiology of the disease and the pathogenesis of the lesion. He states that the main ætiological possibilities to be considered are: (*a*) invasion of the brain tissue by bacteria or virus, (*b*) direct action of circulating toxins on the brain tissue, and (*c*) acquired sensitivity of the brain tissue to a circulating antigen. In regard to the first of these possibilities, he points out that bacteria have not been demonstrated and that no search for a virus has been reported. However, in one of his three cases some cerebral tissue was obtained immediately after death, and two injections of this material were given into the thalamic areas of a rhesus monkey. The monkey showed no abnormal signs apart from slight pyrexia for two days. It was killed thirty-one days after the first injection, but the brain and cord showed no evidence of disease. Passage was not carried out. The structural lesions, he points out, and their distribution are unlike the findings in any known virus disease. The possibility of direct toxic action is, he holds, supported by an observation of Hurst's that chronic cyanide poisoning in monkeys could lead to focal demyelination. In none of the cases of the disease reported has there been any evidence of direct toxic action of this kind. Crawford thinks that the third possibility, that of acquired sensitivity to a circulating antigen, has certain points in its favour. He points out that the lesions are similar to those seen in arsphenamine encephalitis. D. S. Russell, in 1937, described three cases of that condition and drew attention to the evidence suggesting that it was a sensitization phenomenon. More recently, J. B. Cavanagh has described somewhat similar lesions in a patient who died with evidence of hypersensitivity following the administration of streptomycin and para-amino-salicylic acid. The vascular lesion resembles closely that occurring in *polyarteritis nodosa* and producible experimentally in animals by the repeated injection of foreign protein. The demyelination can be imitated experimentally in animals by multiple injections of emulsions of brain tissue with or without certain adjuvants. Crawford points out that the dangers inherent in assuming that similar histological lesions are of similar pathogenesis are well known. At the same time, he adds that this similarity of the lesions in the human disease to experimental hypersensitivity lesions and to lesions occurring in drug sensitization is the only positive guide to ætiology in the disease under discussion. Those who are particularly interested in this condition should read the discussion by Hurst in his article in 1941. It is important that pathologists shall be fully aware of the characteristics of this condition and, for that matter, that clinicians should also know of its occurrence. It will be remembered that Hurst stated that had there been a neurological clinic in Adelaide at the time of his reporting the condition, still further cases would have been detected.

[1] *J. Clin. Path.*, February, 1954.

AN ATHLETE'S VIEW OF SPORT.

FEW top-ranking athletes are competent to write an article on sport appropriate to the pages of a medical journal, but when an athlete has studied his sport scientifically for some years to such purpose that he reaches the world's headlines for breaking the time of four minutes for the mile run, then we can scarcely help being interested in what he has to say. Roger Bannister, who is already a master of arts and a bachelor of science and is in his final year of medicine at Oxford, may be quite reasonably described as taking his sport seriously, but judging from his remarks in a recent article on stress in sport[1] no one could accuse him of regarding it as a business. Discussing the original purpose of sport before the Greeks introduced an "almost religious reverence for physical perfection", he suggests that it was presumably as practice for hunting and war. Nowadays, however, it is "a diversion with no purpose beyond providing a testing ground larger than a chess board but smaller than life itself". He states that the satisfaction to be derived from

[1] *Practitioner*, January, 1954.

sport is incidental to the game, but further analysis indicates that it must result from the need to resolve tension within ourselves. Sport takes the players from rest to activity, from comfort to stress, and its joy lies in the integration of body and mind in simultaneous tension. Unlike art, it tends to be stifled by disease and war. Sport imposes stress on both mind and body, and tests three different abilities: the ability to exert muscular force over a particular distance and time (this is strength or power); the ability of neuro-muscular coordination, which is reflected in the agility, skill and judgement with which individual movements are performed and the smoothness with which they are moulded into a complete pattern; the judgement at a higher level with which the whole behaviour pattern necessary for the game is planned. All sports and games test different combinations of these three abilities. An important and wider problem is motivation, for, as Bannister states, the moment when we cease to care whether our team wins or loses, mental and physical stress disappear. These, however, are psychological rather than physiological problems and need not detain us now.

Turning to the question of factors responsible for the athlete reaching a breaking point under the stress of severe exertion, Bannister states that on the running track there is no absolute limit in theory to any physical performance, but various physiological factors cause a steady diminution in the margin by which records are broken. The sprinter is limited mainly by such factors as muscle viscosity—an innate property of muscle which is affected little, if at all, by training. The provision of oxygen for his muscles is unimportant; in the very short time at his disposal he must rely on the energy provided by less efficient anaerobic mechanisms, which result in the accumulation of lactic acid, sometimes to very high levels. In distance running, on the other hand, reduced oxygen saturation of the arterial blood seems to be the most important primary factor which prevents a man from running faster for a longer time. Oxygen lack is found to affect adversely both the mind and the body. A different stress, which the athlete faces if he continues running for several hours, is a fall in blood sugar concentration. Bannister refers to the remarkable capacity for adaptation of the body in stamina tests, but states that the adaptation is slight when speed is the main factor concerned, sprinters being born, not made. It should be noted, however, that although the body reacts to a moderate stress stimulus by an improvement in stamina, too great a stimulus leads to breakdown. The training adopted by modern distance runners imposes on the body an intermittent stress of oxygen lack. The component factors of the oxygen transport mechanism are integrated during exercise in order to bring about an increase in oxygen uptake. The rate of oxygen uptake by the muscles themselves increases and is coupled with increases in the cardiac output, the speed of oxygen diffusion across the pulmonary epithelium, and the ventilation rate of the lungs. As a result of these changes the muscle fibre receives about fifty times the amount of its oxygen supply when at rest. In sports in which neither speed nor stamina is the objective, for example, weight-lifting, repetitive static exercise causes muscular hypertrophy but not a proportionate increase in blood supply. Sometimes the adaptation to stress is carried so far that the efficiency of the body is reduced in another direction, and Bannister points out that the distance runner does not normally make a favourable impression at a medical examination. He may be nervous and sweating, with an irregular pulse—signs of increased activity in the cardio-inhibitory centre. He will probably have an enlarged heart with increased residual blood in the left ventricle, a low blood pressure and retarded circulation—in fact, he has many of the signs of a diseased heart; yet exercise brings him quickly to a state of extreme sympathetic activity and circulatory efficiency.

On the question of sport and health Bannister points out that there is no evidence that sport promotes increased resistance to disease. On the other hand, a good deal that is misleading has been said about the possible harmful effects of exercise. Bannister considers that the resilience of the school boy is such that he is unlikely to come to any serious harm as the result of strenuous exercise. The factors producing the so-called burnt-out athlete may well be quite natural. A boy's growth-spurt while he is at school may be accelerated, so that he has an unnatural advantage over others in his age group. Later he may develop a physique which has "bloomed" too much in the direction of height, muscle or fat to be successful at his event. Alternatively, the mental strain of excessive competition may make him lose his enthusiasm for the sport. Much more commonly, athletes develop other interests that take them away from the running track, and, of course, such things as a muscle injury may force the retirement of an otherwise fit lad. Bannister also refers to the mistaken view that sudden death in athletes is due to overstrain and to surveys which have shown that athletes and oarsmen live as long as their more sedentary contemporaries. In this regard, we may refer in passing to the recently published investigation into the longevity of Cambridge sportsmen by Sir Alan Rook.[1] Rook found no evidence that sportsmen died at an earlier age than the members of a control group chosen at random, and no evidence could be adduced from the information available that cardio-vascular causes of death were more prominent in sportsmen or occurred at an earlier age. Of course, as Bannister points out, sportsmen may be exposed to incidental risks as they grow older. They may be tempted to indulge in athletic exercise unsuitable for their age, or to continue overeating when it is no longer coupled with exercise; but the results of such unwise activity can scarcely be used as a charge against sport.

OCCULT CARCINOMA OF THE BREAST.

ALTHOUGH its occurrence is rare, occult carcinoma of the breast needs to be borne in mind. The term is used in a recent study by H. W. Owen, M. B. Dockerty and H. K. Gray[2] to imply histologically proved carcinoma of the breast with axillary nodal involvement in a patient who has manifested no signs or symptoms of any abnormality of the breast. The study is based on clinical and pathological material from cases recorded at the Mayo Clinic in the period from 1907 to 1950. Altogether there were reviewed 5451 operative cases of histologically proved carcinoma of the breast in which there was axillary node involvement. Of these, 27 fulfilled the criteria necessary for the diagnosis of occult carcinoma of the breast—an incidence of slightly less than 0·5%. Since involvement of the axillary nodes is encountered in about 66% of all cases of mammary carcinoma at the Mayo Clinic, it would appear that approximately 0·3% of all patients with carcinoma of the breast have the occult form of the disease. It is interesting to note that there was one man in the group, although only 1% of all cancers of the breast occur in the male, and one would expect a reduced possibility that carcinoma of the breast would be occult in the male. However, it is not difficult to understand why the lesions in this series were occult, even in the one male patient, when we learn that their size ranged downwards from a diameter of less than ten centimetres to a diameter of only microscopic dimensions. Moreover, most of the lesions were deep within the breast tissue, and in some cases their presence was masked by fibrous mastitis producing generalized thickening of the breast. A large percentage of the lesions were of the comedo type, and in a significant number of cases the so-called inflammatory reaction was present about the tumour. The presence of this reaction has been stated to signify a better prognosis, but no conclusion on this could be drawn from the present study. Owen, Dockerty and Gray state that the outstanding feature in this series was the complete lack of signs and symptoms pointing to the existence of a primary cancer in the breast. The presence of an axillary tumour, with or without symptoms referable to the breast, should

[1] *Brit. M. J.*, April 3, 1954.
[2] *Surg., Gynec. & Obst.*, March, 1954.

therefore cause the patient to seek medical care. Another investigator, C. S. Joss, is quoted as finding that metastatic carcinoma was the most frequent single cause of apparent primary enlargement of the axillary lymph nodes, the possible primary sources of the lesion being a small primary focus in the breast, carcinoma of the tail of the breast extending into the axilla, carcinoma in accessory axillary tissue, small non-pigmented melanoma, and tumours of the lung and pleura. No definite information could be found in the literature on the relative frequency with which occult carcinoma of the breast and other occult primary tumours were associated with metastatic carcinoma of the axillary nodes.

The recommendations for treatment of occult carcinoma of the breast are described by Owen, Dockerty and Gray as being dependent on the knowledge that there often exists within the homolateral breast a lesion of such small size that its detection is clinically impossible. Definite enlargement of the axillary nodes is therefore an indication for biopsy. If there is metastatic adenocarcinoma in the glands, a primary source must be searched for. How often the primary focus will be in the breast is not clearly known, but it must be considered as the most likely source, especially in a woman. The view is expressed here that a thorough search for other metastatic foci should be made, and if no focus is found and if no further evidence of spread exists, the treatment indicated is the same as for any carcinoma of the breast with axillary nodal metastasis, namely, radical mastectomy. The authors state that a primary focus of carcinoma may not be found in the removed breast. On the question of prognosis, Owen, Dockerty and Gray are reluctant to draw any conclusions from their relatively small series, but there is a suggestion that the prognosis is better than accompanies the average carcinoma of the breast with nodal metastasis.

CHANGES OF SEX.

IT is disturbing to find such crude weapons as œstrogens and plastic surgery being regarded as an answer to a problem at once so common and so subtle as that presented by aberrations of the sexual pattern discussed recently in the popular Press. These same weapons were used for some time in the treatment of another sexual disorder, female pseudohermaphroditism due to congenital adrenal hyperplasia. L. R. Broster, J. Patterson and B. Camber have recently reviewed their results from surgery in this condition and even their strangely optimistic paper[1] does not conceal how little adrenal surgery has to offer these unfortunate girls. In 1951, L. Wilkins *et alii* reported the results of short-term intramuscular administration of cortisone to ten patients with congenital adrenal hyperplasia.[2] Reduction of androgen excretion was achieved in all, and signs of feminization appeared in several girls. These workers and several others have since published papers showing that these favourable results can be maintained for long periods. One of the most recent of these reports comes from Sydney, where Robert Vines and Lorimer Dods have given cortisone to six children suffering from female pseudohermaphroditism due to congenital adrenal hyperplasia.[3] Their results were uniformly favourable. The older girls lost their acne and hirsutism, developed breasts and began to menstruate, while the rapid growth and skeletal maturation and increasing hirsutism of the younger girls was halted. A salt-losing tendency, causing weight loss, dehydration and prostration, was present in the two infants of this series. Extra salt and injections of deoxycortone, in addition to cortisone, were necessary to control this tendency and to preserve life. There seems little doubt that, backed by suitable experience and biochemical control, cortisone has much to offer these unfortunates. That the condition deserves always to be kept in mind is shown by the fact that in the last eight years Lorimer Dods has encountered fifteen such cases, while during that time six more subjects have been examined in the post-mortem room of the Royal Alexandra Hospital for Children, Sydney.

[1] *Brit. M. J.* (1953), 2: 1288.
[2] *J. Clin. Endocrinol.* (1951), 11: 1.
[3] *Australasian Ann. Med.* (1954), 3: 5.

MAGNESIUM DEFICIENCY IN RELATION TO CHRONIC ALCOHOLISM.

THE manifestations of magnesium deficiency have been well defined in various species of animals, but little is known about the effects of deficiency in man. *Delirium tremens* has been treated empirically with magnesium sulphate given parenterally with success, but the reason for giving it was the sedative action of magnesium salts. E. B. Flink, F. L. Stutzman, A. R. Anderson, T. Konig and R. Fraser[1] have studied the occurrence of magnesium deficiency in cases of chronic alcoholism complicated by *delirium tremens* and after prolonged parenteral fluid administration in other patients. Cows with grass tetany (or staggers), which is a magnesium deficiency disease, are restless and nervous, lack appetite, have muscle twitching, unsteady gait, gnashing of the teeth and rolling of the eyes, with an anxious and wild look. Soon tonic and clonic convulsions appear, followed by a paretic or comatose state. Calcium chloride and magnesium chloride given intravenously cause rapid improvement. Many of these symptoms were demonstrated in the patients studied in this paper, whose blood magnesium content was below normal. Gross tremor, athetoid and choreiform movements of the extremities and twitching of the face were characteristic. Convulsions occurred in some patients, also delirium. Varying degrees of confusion, disorientation, hyperactivity, hallucinations and delusions occurred. The lowest magnesium concentrations occurred in very ill patients and there was some correlation of severity of manifestations and the magnesium concentration. All patients with magnesium concentrations below the normal range have not shown the symptoms described. Apart from alcoholics, who show deficiency because alcohol has been almost the sole source of calories, patients receiving fluids parenterally for a long time may develop magnesium deficiency and have gross muscular tremor and delirium. While most patients with *delirium tremens* recover when they are given sedatives and begin eating, much earlier recovery was usually seen when magnesium sulphate was given intramuscularly. Two grammes of magnesium sulphate (50% solution) were given intramuscularly four times a day for three days, then 1·0 gramme for two to four days. One gramme of magnesium sulphate contains 99 milligrammes of magnesium. Oral administration of magnesium salts was not tried, but it should be effective, as magnesium is considerably absorbed from the intestine and 40% of an oral dose appears in the urine.

[1] *J. Lab. & Clin. Med.*, February, 1954.

ASCORBIC ACID AND ADRENAL CORTICAL ACTIVITY.

IT is recognized that ascorbic acid plays an important although ill-defined part in the activity of the adrenal cortex. It is found in high concentration in the adrenal glands, anterior pituitary lobe and *corpus luteum*, but disappears rapidly from the adrenals of animals exposed to various kinds of stress. As long ago as 1947, C. N. H. Long, in a paper to which reference was made in these columns,[2] described the prompt fall in the level of ascorbic acid in the adrenal which follows injection of corticotrophin (ACTH). These facts are not understood, although, as H. H. Khalil[3] has pointed out, the degree of depletion has been used for quantitative biological assay of adrenocorticotrophic activity. It has been suggested that ascorbic

[2] M. J. AUSTRALIA, February 14, 1948.
[3] *Lancet*, May 1, 1954.

acid and cholesterol are concerned with the production of the cortical hormones, and also that ascorbic acid may in some way be incorporated to render the steroid hormones water-soluble; but there is no agreement on these points. It is interesting to note the effect of hypophysectomy on adrenal cortical activity. Hypophysectomy in the rat results within a few days in pronounced reduction of the adrenal weight. Khalil states that histological examination of sections of the adrenal glands in such a case shows atrophy of the *zona fasciculata* and *zona reticulata*, and the glands lose their high degree of sensitivity to corticotrophin. The administration of corticotrophin as replacement therapy can prevent this atrophy. Khalil has investigated experimentally the possibility that the high concentration of ascorbic acid in the adrenal glands may have a role in maintaining the adrenal weight. Twenty rats were subjected to hypophysectomy and divided into two equal groups; ten were given a daily intravenous injection of 100 milligrammes of sodium ascorbate in saline, and ten were given the same volume of saline by intravenous injection. After a week all twenty animals, as well as a group of ten intact animals, were killed and the adrenals weighed. The adrenal weight of the saline-treated hypophysectomized rats was very much less than that of the ascorbate-treated hypophysectomized rats, and the difference was considered to be statistically significant. The adrenal weight of the ascorbate-treated hypophysectomized rats was a little less than that of the control rats, but the difference was barely significant. In other words, the reduction in adrenal weight which normally follows hypophysectomy and is prevented by administration of corticotrophin can be almost averted by means of ascorbic acid alone.

These are, of course, isolated findings, and their place in the total picture of adrenal cortical activity cannot yet be determined. At present it can be said only that they give greater prominence to the place of ascorbic acid in this activity. Further work is now in progress to find out whether ascorbic acid has any potentiating effect on the increase or maintenance of adrenal weight which is produced by administration of corticotrophin to hypophysectomized rats.

CONTROLLED HYPOTHERMIA AND CARDIAC SURGERY.

REDUCTION of the body temperature during anæsthesia is a technique which has proved of most value in cardiac surgery. The most convincing demonstration of this was by H. Swan and his colleagues[1] in Denver, who wrote on surgery by direct vision in the open heart during hypothermia. Patients require less oxygen with a reduced body temperature, and in practice this allows a much longer time during which intracardiac surgical operation can be performed, as the risk of permanent cerebral damage from arrest of the circulation is diminished. J. McNaught Inglis, W. H. Bitten and A. L. d'Abreu[2] have recently designed an apparatus which allows hypothermia to be controlled with ease. It is obviously desirable to have an accurate regulation of rate and degree of cooling, and the possibility of cardiac irregularities at low temperature made the authors seek a method by which they could institute rewarming at any time during the operation. Their apparatus consists of a hypothermia unit from which fluid is pumped along tubes wrapped in a blanket. The fluid circulates through the tubing and returns to a central reservoir tank which contains cooling coils and immersion heaters. The circulation is variable and may be stopped whilst the temperature of the tank under thermostatic control is altered. The authors have used hypothermia in the treatment of seven children aged from four months to thirteen years, and have had no difficulty in either cooling or rewarming the patients; both these processes they found take place at about the same rate. Their technique is to fold the blanket so that it contains an air space and then to seal the ends. The temperature of the contained air is reduced to 5° C. in about thirty minutes. The patient is anæsthetized with rectally administered thiopentone and with nitrous oxide and oxygen and small doses of pethidine. Complete curarization with d-tubocurarine is recommended not only for controlled breathing, but also to prevent shivering. A rectal or œsophageal thermocouple is connected before the child is placed in the cold lumen of the blanket, and the ends of the lumen are again sealed as far as possible. The rate of cooling will depend on the size of the patient, the temperature gradient and the degree of vasoconstriction; with a two-year-old child it is about 10° C. an hour. When the patient has been cooled, the amount of anæsthetic agents required is considerably reduced. When the desired temperature of about 25° C. is reached, the blanket is opened and the operation performed with the child lying on it. Circulation through the tubes can usually be stopped once the operation has begun, whilst the temperature in the tank is raised from 5° C. to 45° C. in preparation for rewarming, which is merely a reversal of the previous process. Whatever its place in general surgery, this technique of hypothermia has an assured position in surgery of the heart.

[1] *J.A.M.A.*, November 21, 1953.
[2] *Lancet*, March 13, 1954.

WASP VENOM.

LITTLE is known about the toxic constituents of insect venoms. R. Jaques and M. Schachter[1] have examined the venom of the common English wasp and have separated three toxic substances. The entire venom apparatus of the wasp was dissected from a number of wasps, dried and extracted with water. About 30% of the dried material was dissolved in the extract and was taken as representing the venom. The extract was examined by chromatography and three constituents were separated. These were found to be histamine, 5-hydroxytryptamine and an unidentified potent smooth muscle stimulant. The histamine was present in a concentration of 16 to 20 milligrammes per gramme of dried venom. Since histamine concentration of 1 in 1000 causes pain when applied to a blister base in human skin it can be inferred that the injection of histamine by the wasp contributes to the pain and œdema following a wasp sting. Similarly, the minimum possible concentration of 5-hydroxytryptamine in venom was of the order of 0·32 milligramme per gramme, which would be a greater concentration than the pain-producing threshold of this substance for human skin. These two substances then will account for some features of the human skin reaction following a wasp sting, but other factors are undoubtedly involved. A highly potent substance which produced a delayed, slow contraction of the guinea-pig ileum in a concentration of 1 in 3,000,000 was also isolated. This substance resembles, in many of its properties, bradykinin, obtained by incubating globulin with snake venom or trypsin, and which may be a polypeptide produced by the proteolytic breakdown of globulin. The venom also contains large amounts of hyaluronidase, which would enhance the diffusion of toxic substances in the skin. Some specimens of venom also release histamine in the skin—that is, in addition to what is injected. Histamine is known to be widely distributed in animal tissues. There is more recent evidence that 5-hydroxytryptamine is also widely distributed, for example in the mucosa of the mammalian gastro-intestinal tract and spleen. Histamine, 5-hydroxytryptamine and bradykinin have been demonstrated during the anaphylactic reaction. It seems probable that the reactions caused by the stings of the Portuguese man-o'-war (Physalia) are due to one or more of these substances, particularly histamine, for the sea anemone secretes a substance which liberates histamine.

[1] *Brit. J. Pharmacol. & Chemotherapy*, March, 1954.

Abstracts from Medical Literature.

OPHTHALMOLOGY.

Intraocular Pressure in Primary Congestive Glaucoma.

S. J. H. MILLER (*Brit. J. Ophth.*, January, 1953) investigated 100 individuals who suffered from glaucoma characterized by a clinical onset consisting of periodic haloes with episodes of blurred vision and ocular pain. Narrow angles, full peripheral and central fields of vision, and absence of cupping of the optic disk in the early stage of the disease were the main ocular features. The author states that when the diagnosis is in doubt a patient who complains of periodic haloes should be instructed to report for tonometry during an attack, for at that time the pressure will be raised. The cinema and television are the commonest provokers of attacks, and it is rare for a patient with congestive glaucoma to deny the detrimental effect of the cinema on visual acuity. Emotional crisis and prolonged visual concentration may precipitate attacks. Sleep and rest tend to lower a raised intraocular pressure. The author compares simple and congestive glaucoma in respect to clinical features and variation in intraocular pressure. Congestive glaucoma tends to occur in women, affecting eyes with narrow angles. Simple glaucoma occurs in either sex, affecting eyes with wide, medium or narrow angles. In the congestive group the onset is acute or subacute, and in simple glaucoma it is insidious. The visual fields, usually unaffected in congestive glaucoma, show much change in the simple type. Similarly, the disk is normal in the congestive and cupped in the simple type. The rises in intraocular pressure in congestive glaucoma are periodic, the frequency of attacks increasing as the disease progresses, and the variation between maximum and minimum pressures diminishes as the disease progresses. In simple glaucoma the diurnal variation curve of intraocular pressure repeats itself faithfully from day to day, and the higher the maximum tension, the greater the variation between this and the minimum tension. The factors which precipitate rises in tension in congestive glaucoma have no effect in simple glaucoma. The destruction of the eye as a seeing organ is related in congestive glaucoma to the number and duration of the attacks of raised pressure, whereas in simple glaucoma fields are destroyed without the accompaniment of a high intraocular pressure. In the later stages the two types of glaucoma may be so alike as to be indistinguishable.

Toxoplasmosis in the Adult.

S. DUKE-ELDER *et alii* (*Brit. J. Ophth.*, June, 1953) report on a case of relapsing acute choroiditis in a man, aged forty years. The lesion was regarded as tuberculous, and histological diagnosis after enucleation indicated that it was probably tuberculous. Two years later the authors reviewed the sections and carried out tests on the patient for toxoplasmosis. The sections showed crescentic structures morphologically indistinguishable from toxoplasma. The findings of serological tests were significant, and when they are taken in conjunction with the histological findings there can be little doubt that the granulomatous chorioretinitis was toxoplasmic in origin. Before a case of choroiditis is regarded as even probably due to toxoplasmosis it is necessary to observe typical histological forms and to demonstrate positive serological test findings.

Non-syphilitic Interstitial Keratitis, Bilateral Deafness and Essential Polyangiitis.

LEO OLINER *et alii* (*New England J. Med.*, June, 1953) review Cogan's syndrome, which consists of non-syphilitic interstitial keratitis with deafness. They state that the syndrome usually occurs in young adults and is of sudden onset, with either ocular or aural symptoms. The presenting ocular symptoms may include redness of the eye, blurring of vision, ocular pain, lachrymation, blepharospasm and subconjunctival hæmorrhage. Both eyes may be involved. The vestibulo-auditory signs resemble Ménière's syndrome; they appear suddenly with nausea, vomiting, tinnitus, vertigo and rapid development of deafness. With the onset of deafness the associated vestibular signs diminish. The symptoms of both systems may occur within a few hours of each other, or there may be an interval of up to five months. Usually the interval consists of one to two weeks. Early there is a granular type of corneal infiltrate, patchy in distribution and found predominantly in the posterior half of the cornea. The endothelium of the cornea may be boggy. Later the cornea is vascularized. There may be poor response to mydriatics, and paralysis of extraocular muscles may occur. There is inner ear deafness, unilateral or bilateral. The syndrome runs a chronic course with multiple unpredictable recurrences. The cause of the syndrome is unknown. The authors describe a case in which the clinical picture of *periarteritis nodosa* developed. They incline to the view that the syndrome is only a localized manifestation of essential *periarteritis nodosa*.

Pre-anæsthetic Sedation and Analgesia.

WALTER S. ATKINSON (*Arch. Ophth.*, May, 1953) discusses various sedatives and analgesics in common use in intraocular surgery. He states that the barbiturates are excellent sedatives for use prior to intraocular operations because they rarely cause nausea, vomiting or other undesirable effects. All barbiturates have the same general type of depressant action on the central nervous system, but recovery from an overdose may be accompanied by restlessness, during which the patient may be irrational and hyperactive. Patients with an idiosyncrasy may become excited and as unmanageable as a patient with acute alcoholism. Chloral hydrate is an excellent alternative to the barbiturate, and it rarely causes excitement or delirium. Morphine is contraindicated for intraocular surgery because it frequently causes nausea and vomiting. A large number of eye surgeons are using meperidine hydrochloride in addition to barbiturate for pre-anæsthetic medication. It has potent analgesic properties, a slight sedative action and an antispasmodic effect. The dose of meperidine hydrochloride for an average adult of 70 kilograms is 50 to 150 milligrammes. The drug is given by intramuscular injection but may be given orally. When it is given intramuscularly the analgesic effect is apparent in fifteen minutes, with a maximum effect in forty-five to sixty minutes. The drug is well tolerated and rarely produces toxic reactions in therapeutic doses. To prevent nausea the author recommends the use of an antihistamine. He recommends that a test dose of the drugs be given the day before operation to make sure that there are no untoward side-effects. The author recommends "Nembutal" 100 milligrammes, meperidine hydrochloride ("Demerol") 25 milligrammes, and "Phenergan" 12·5 milligrammes the evening before operation, and "Nembutal" 100 to 200 milligrammes with meperidine hydrochloride 50 to 100 milligrammes one and a half hours before operation. A further dose of "Nembutal" can be given at the end of one hour. "Phenergan" is given two hours before operation.

Diabetic Retinopathy Treated with Testosterone.

ROBERT H. BEDROSSIAN *et alii* (*Arch. Ophth.*, September, 1953) conducted a well-controlled experiment in which they were able to assess the effect of testosterone on diabetic retinopathy. Patients were divided into three groups. One group, which served as a control, received an injection of saline, the second group received 50 milligrammes of testosterone, and the third group received 50 milligrammes of testosterone and 2·5 milligrammes of œstradiol. The patients' fundi were examined at intervals of five and fifteen weeks, and final evaluation was made after seventeen to twenty-four weeks of therapy. The patients' diet and their insulin management received the usual clinical control. Statistical evaluation by the usual methods failed to show that the hormone therapy was of more benefit than the saline treatment.

Gonioscopy in Foreign Bodies of the Chamber Angle.

HERBERT L. MOSKOWITZ (*Arch. Ophth.*, September, 1953) reports two cases to demonstrate the value of gonioscopy in diagnosing the presence of foreign bodies in the angle of the anterior chamber. He states that the clinical manifestations of foreign bodies retained in the anterior chamber angle depend in great part on the composition and chemical activity of such objects. Copper and iron are poorly tolerated, their presence leading to chalcosis and siderosis. Nickel, chromium, zinc and lead are less active, while gold, silver, and stainless steel may be well tolerated. Non-metallic particles—sand, stone, glass and "Bakelite"—may produce little or no response. A retained foreign body may be the cause of anterior uveitis, and in all such cases, especially those in which there has been any trauma, the patient should be subjected to gonioscopic examination, as there may be a retained foreign body in the chamber angle.

Surgery of Congenital Glaucoma.

OTTO BARKAN (*Am. J. Ophth.*, November, 1953) reviews the results of goniotomy performed on 196 eyes and discusses diagnosis and operative technique. He draws attention to the importance of measuring the tension; he states that complete relaxation of the child is essential, and this is best achieved under ether anæsthesia. The

disk and fundus often appear blurred owing to irregular astigmatism, but viewed through the contact glass the fundus picture is clear. In the cases which were successfully operated upon reduction in visual acuity was caused by corneal scars, irregular astigmatism, ruptures in Descemet's membrane or amblyopia, the result of interruption of development of central vision during infancy. The author operates under direct vision, using a contact lens, and makes a plea for early operation. For infants only a few days old he operates on one eye immediately, after preliminary deepening of the anterior chamber, and on the second eye after two to four weeks have elapsed. The operation is contraindicated in the late distended stage of buphthalmos, but has been used successfully in glaucoma associated with aniridia and *nævus flammeus*.

Biopsy of Iris Neoplasms.

DANIEL B. KIRBY (*Am. J. Ophth.*, September, 1953) describes a technique for total biopsy of neoplasms of the iris and gives indications for the procedure. If the lesion is slowly growing and isolated, and particularly if it is not involving the angle or ciliary body, if the pupil is not distorted, if the mass is single, if transillumination verifies location and extent, if the lesion is in the inferotemporal area of the iris, and finally if it is salmon-coloured or flesh-coloured, then total excisional biopsy is indicated, as the neoplasm may well be a leiomyoma. The author makes a large ab-externo incision at the limbus and, when half-way through, places sutures through the corneal lip. The incision is completed and enlarged with scissors. The sutures are now used to elevate the corneal flap. The normal iris is grasped with iris forceps two millimetres from the tumour, buttonholed, and incised through the sphincter and then through the base; this is followed by drawing the iris and tumour centrally while the incision is being carried along the base. After the tumour area has been passed, the line of incision is turned radially toward the pupil and total excision completed. The limbus incision is now sutured.

OTO-RHINO-LARYNGOLOGY.

Perception Deafness and Tetanus Antitoxin.

M. D. BERGER AND A. R. SACKS (*Arch. Otolaryngol.*, May, 1953) state that the ætiological factors in the causation of perceptive deafness are many and varied. The cause is often obscure. Of the neurological complications associated with serum injections more than 50% have followed the prophylactic use of tetanus antitoxin. The pathological process which occurs is not fully clear. Four cases of auditory nerve involvement after the use of tetanus antitoxin have been previously resported. In two of these cases large doses of the serum had been given for clinical tetanus. In the other two cases deafness occurred after the prophylactic use of tetanus antitoxin and was preceded by serum sickness. In the authors' case generalized giant urticaria developed one week after the prophylactic injection and was followed the next day by sudden severe deafness, which persisted. The authors state that in all probability the damage which occurs is part of the serum sickness effect. Any patient with serum sickness showing a tendency to tinnitus, vertigo or impaired hearing requires immediate therapy. The early use of adrenaline, antihistamines, cortisone and possibly intravenous histamine therapy should be thought of in an effort to prevent serious damage.

Surgical Repair of the Perforated Ear Drum.

H. P. HOUSE (*Ann. Otol., Rhinol. & Laryngol.*, December, 1953) states that in a patient who was troubled with tinnitus and who had a large tympanic perforation, it was planned to resect the tympanic plexus off the promontory and to apply a thin full-thickness skin graft over the middle ear region. The tinnitus was unrelieved, but the graft healed in its entirety. In a patient undergoing a fenestration operation the tympanic membrane was torn extensively. It was decided to curette the promontory immediately and to apply a thin full-thickness graft over the area. Radiating incisions were made in the remaining ear drum out to the annulus, so that the marginal flaps dropped to the promontory. A free skin graft was then applied over all. When dressings were removed on the fifth day, a healthy-appearing skin graft was found to be adherent to the promontory; and since the ear drum remained mobile between the graft edges and the annular ring, a small peripheral but sealed middle ear space was created. Later the drum had released itself from the promontory and was again entirely mobile. In two other cases the ear drum remained adherent to the promontory.

One-stage Radical Resection of Cervical Structures.

J. J. CONLEY (*Arch. Otolaryngol.*, December, 1953) states that a one-stage operation of radical resection of the cervical part of the œsophagus, larynx, pharynx and lateral region of the neck has been developed in the hope of mitigating the morbidity encountered with multiple-stage methods and delayed reconstruction. The one-stage operation consists of radical resection of the cancerous growth and immediate reestablishment of continuity between the pharyngeal stoma and the cervical part of the œsophagus by the careful anastomosis of a tube of free thick split skin, which is formed into a tube over a stent of wire mesh or plastic material. With the use of antibiotic agents the fear of loss of the graft by infection is greatly lessened. Laryngectomy and the necessary degree of cervical œsophagectomy are performed in continuity, together with block dissection of the neck where necessary. The free skin graft is rolled into a tube two centimetres in diameter at its lower end and four centimetres for its pharyngeal attachment, the length being such as to fill the void between the upper and lower openings. The tube is sutured with number 00 chromicized catgut, and this longitudinal suture line is placed against the prevertebral fascia to ensure a maximum amount of nourishment and the greatest amount of tissue support. Careful anastomosis of the free skin tube to the circumference of the pharyngeal and œsophageal mucosa is carried out with number 00 chromicized catgut so as to eliminate saliva from the neck wound. The stent, which is used essentially to prevent stenosis, must comfortably fit the wound, else its extrusion is likely. It is desirable that the stent should remain *in situ* for at least six months. In closing the neck wound efforts are made to cover the tube of skin with supporting and nourishing tissues, such as prevertebral fascia and the lobes of the thyroid gland. The skin flaps are then replaced over the entire wound area and sutured with fine silk. Feeding is through a fine tube for ten to fourteen days, after which sterile liquids are cautiously taken by mouth. If there is any leakage, the feeding tube is retained until healing is complete. Stenosis is the most unpleasant complication and may appear gradually after many weeks or months. Generous cutting of the grafts and avoidance of infection are two important factors in ensuring against stenosis. Bouginage may be necessary and is helpful should stenosis develop. Recurrence of cancer must be considered.

Thyrotomy Approach for Arytænoidectomy.

S. J. PEARLMAN AND E. W. KILLIAN (*Ann. Otol., Rhinol. & Laryngol.*, March, 1953) report four cases of bilateral abductor paralysis of the vocal cords treated by arytænoidectomy through laryngo-fissure (thyrotomy). The operations were successful in that all patients were given an adequate airway and retained useful voices.

Aureomycin and Nicotinic Acid for Ozæna.

H. ROSEN, S. FELDMAN AND M. MADORSKY (*Ann. Otol., Rhinol. & Laryngol.*, March, 1953) state that an encapsulated Gram-negative bacillus, very similar to Friedländer's bacillus and classified as Klebsiella, has been repeatedly found by many authors in cases of ozæna. Its ætiological part in the disease, however, remains unproven. Other organisms, such as a Gram-positive bacillus of the Corynebacterium group, Perez's bacillus and *Pseudomonas æruginosa* and different Gram-positive cocci, have been found as well. Aureomycin was chosen by the authors in view of its antibiotic effect against Klebsiella organisms, and nicotinic acid on account of its vasodilator effect. The study included 11 patients with well-established disease. The method of treatment consisted of daily oral administration of 250 milligrammes of aureomycin at six-hourly intervals. Simultaneously, nicotinic acid was administered orally in doses of 50 milligrammes three times daily, and in addition 50 milligrammes were administered intravenously. None of the patients was allowed to use local treatment or nasal irrigations. The immediate result was very impressive. In 10 of the 11 great improvement occurred. Crusting and fœtor disappeared in eight of these 10 cases. Atrophy and anosmia were but little affected. Many of the previously detected bacteria disappeared in subsequent culture tests. In contrast with the immediate satisfactory condition the subsequent results were disappointing. Commencing about four weeks after cessation of treatment, relapse to the former condition gradually occurred in most cases. It is felt that a more prolonged form of maintenance treatment may be needed. The use of a 3% aureomycin ointment applied locally in the nose is also undergoing trial.

Special Articles for the Clinician.

(CONTRIBUTED BY REQUEST.)

CI.

THE INVESTIGATION OF ASTHMATIC PATIENTS.

THE main objects of investigation of an apparently asthmatic patient are to make sure that the patient's illness is really asthma and then to determine as clearly as possible the type of asthma, causes, mechanism and prognosis. In this article it will be possible only to touch briefly on the more important aspects.

Differential Diagnosis.

Other conditions associated with dyspnœa occasionally cause confusion. As a rule a well-taken history and careful clinical examination will easily settle the diagnosis, but conditions such as cardiac dyspnœa, hypertension, idiopathic emphysema, bronchitis, chronic nephritis, new growth and foreign body in the bronchus will cause confusion. On the other hand, asthma in infants is frequently diagnosed as bronchitis, bronchopneumonia or even pneumonia, and in adults chronic, mild, persistent asthma is sometimes labelled as chronic bronchitis. Some tuberculous patients also show a definite degree of bronchospasm, which is promptly relieved by adrenaline. So-called "cardiac asthma", which is better described as "paroxysmal nocturnal cardiac dyspnœa", often wakes the patient in the early morning hours, but it is generally met with in men beyond middle age suffering from hypertension. A cautious dose of adrenaline gives no relief or aggravates the condition, and it should not constitute much of a difficulty in diagnosis. True asthma is generally relieved by one or two adequate doses of adrenaline injected subcutaneously. Especial care in diagnosis must be taken when a patient over forty years of age develops for the first time in his life symptoms suggestive of asthma. Most of these patients have hypertension, but some victims of bronchogenic carcinoma exhibit initially true bronchospasm, which is at first relieved by adrenaline.

Mechanism.

The symptoms of asthma are generally thought to be due to bronchiolar spasm, secretion of tough mucus, swelling of the mucosal lining of the tubes and perhaps obstruction of circulation through the lungs. In uncomplicated cases in young subjects these changes are all "reversible", whereas in established cases in older subjects there are usually "irreversible" conditions such as emphysema, loss of lung elasticity, chronic infection, sinusitis and rigidity of the thoracic cage.

Causes.

The success of treatment depends largely on how much insight the physician has into the causes of the patient's illness. Asthmatic attacks are commonly precipitated by exposure to allergens or by infections, but other factors such as reflex irritation, emotional stress and digestive upsets will also precipitate attacks. These precipitating factors will not cause asthma in normal individuals, and numbers of patients have severe infective sinusitis or marked allergy to air-borne factors without ever having asthma. It is necessary therefore to postulate a special "constitutional make-up" or "diathesis" which predisposes the patient to have asthma when the appropriate precipitating factor operates.

The worst possible mistake is to take a one-eyed view of cause. In most cases, several factors combine to produce the disorder, and good results will depend on defining all these and assessing the relative importance of each. The history generally gives a good indication of the main causes, and well-planned investigation enables one then to define and assess these causes.

Types.

Physicians usually divide asthmatic states into two broad types, the "extrinsic" and the "intrinsic". The "extrinsic" cases constitute 70% of all cases in which some air-borne factors such as pollens or domestic dusts precipitate the asthmatic attacks. Practically all these patients when subjected to skin tests show definite allergic reactions, symptoms vary with changes of season or environment, and desensitization, as a rule, produces a great improvement.

On the other hand, cases of "intrinsic asthma" are commonly due to infective sinusitis or to some other internal cause, such as nasal polypi or old nasal injuries. These patients are unable to avoid the cause, which tends to operate fairly continuously. It is difficult to terminate a chronic established infection; so that the prognosis is correspondingly poor, and the asthma tends to be more severe and persistent. About 1% of all asthmatics show "Francis's triad" (that is, nasal polypi, intolerance of aspirin and a low blood pressure), and the prognosis in these cases is extremely bad, because medical treatment seldom helps and any surgical interference with the sinuses tends to make the asthma much worse. These patients rarely show significant allergic reactions, but antibiotics sometimes produce a marked if transient improvement. Food allergy does not seem to be an important cause of asthma in adults.

Investigations.

The three important investigations are a well-taken history, a thorough clinical examination and appropriate tests for allergy.

History.

It is important to decide as quickly as possible about the type of asthma from which the patient is suffering. This is usually settled by asking such questions as: "Do symptoms vary with changes of environment or season?", "Is there hay fever?", "Do the eyes, nose or palate itch?", "Is there infective sinusitis or tonsillitis, or have there been operations on the nose or throat?", "Are head colds frequent?", "Is there post-nasal discharge?", "Is there much sputum?", "What is its colour?", "Is it present only during attacks?", "Do any special dusts, foods or drugs upset the patient?", "Does the patient smoke heavily?", "Are there any relatives with hay fever or asthma?", "Is there a history of previous illness?", "Is the digestion sound?", "Is there emotional stress?", "What is the mode of onset of the illness?", "What gives most relief?", "What previous treatments have been given?", "Do antibiotics or sulphonamides help?".

Clinical Examination.

Before detailed examinations are made a brief talk and inspection (especially of facial expression) is revealing. Is the patient intelligent and likely to follow instructions, or is he stupid and vacillating and incapable of making a fight for health? In long-established cases the patient may show the barrel chest and raised shoulders suggestive of emphysema; whereas, between attacks, patients, in recent cases show practically no abnormal signs or symptoms. During an attack the wheezing and dyspnœa are very typical, and the stethoscope reveals prolonged expiration, expiratory rhonchi and diminished lung ventilation. These signs should disappear almost completely after an adequate dose of adrenaline. In perhaps 5% of cases the rhonchi and prolonged respiration are inspiratory.

If the dyspnœa is continuous and severe, patients often develop pigeon breast. Clubbing of the fingers is not commonly associated with asthma, but should always be looked for, as some patients have associated bronchiectasis.

Some children are febrile during an attack, and the beginner is liable to make a diagnosis of pneumonia. Actually physical signs at the height of an attack are liable to be misleading, and it is wiser to postpone diagnosis of complications for at least a few hours and especially to observe the effect of adrenaline.

Other helpful lines of investigation are an X-ray examination of the chest and nasal sinuses, an opinion from a rhinologist, a differential count of the leucocytes, examination of the sputum, examination of the urine and blood pressure and, sometimes, a test meal examination.

Tests for Allergy.

Allergy is detected by a carefully taken history and by skin tests done either by the scratch or by the intradermal method. Sometimes (for example, in infants) sensitivity is passively transferred by injecting serum from the patient into the skin of a normal non-allergic subject (Prausnitz and Kustner's method). Skin tests with foods are less reliable than tests done with inhaled substances, such as pollens and dusts, and elimination diets may yield more dependable information. If symptoms are very intermittent, a well-kept diary is better, as a patient cannot exist on freak diets for long periods.

Scratch Tests.—A row of tiny scratches or very slight cuts, too shallow to cause bleeding, is made with a scalpel on the skin of the arm, forearm or back, and extracts of the

various dusts and pollens are gently rubbed into these scratches by means of small metal applicators. If dry powdered extracts are used, a drop of carbolized, buffered saline is put on the scratch, and a pinch of the dry material is mixed up with the saline and gently massaged into the cut with a tiny metal spatula. After about five minutes, if the patient is allergic, itching and flushing occur at a few of the test sites, and within about ten minutes definite irregular urticarial weals appear and spread around the sites. These reactions persist for about half an hour and then disappear. The scratches are commonly made about an inch apart, and hairy areas or those strongly tanned by sunlight should be avoided. Scratch tests have the advantage that they are almost painless, they require simple equipment, and they have no dangers for the patient. The allergens commonly tested include animal danders, feathers, kapok, house dust, orris root, linseed, silk, pollens (especially of grasses) and foods such as egg white, milk, wheat, nuts and condiments.

Intradermal Tests.—Intradermal tests can be dangerous, and it should be a rule never to do introdermal tests with potent allergens until the degree of the patient's sensitivity has been defined by preliminary scratch tests. If this rule is ignored, violent constitutional reactions may follow within a few minutes of the intradermal tests, and deaths have occurred in exceptional cases. With a sterile tuberculin syringe fitted with a fine (number 27) short-bevel needle, a minute drop of the sterile liquid extract of a safe strength is injected intradermally. About eight sites are injected in this way, but if any injection is followed by the rapid development of a weal, it is better to desist from further intradermal testing until the degree of reaction has been ascertained. About 0·02 ml of the test material is sufficient for each injection; but a few control tests should first be made with buffered saline, and at these sites about 0·05 ml of saline is injected to ascertain how the skin reacts to injections of bland material. Positive reactions are indicated by a weal, flushing and itching as with the "scratch" tests.

Further details regarding methods of testing for allergy are available in the standard text-books. Obviously much depends on good technique, potent extracts and the intelligent use of controls.

Although the technique of testing for allergy is so simple, experience shows that, in the beginner's hands, it is liable to provide misleading information. It should be an invariable rule to retest the patient once or twice to make sure that he shows the same pattern of sensitivity. All too frequently it happens that hurried and unskilled tests seem to have indicated that a patient is sensitive to a multiplicity of airborne dusts and pollens, whereas retesting often shows that many of these reactions cannot be reproduced. Sometimes patients are subjected to months of expensive treatment with reagents to which they show no sensitivity at all. Extensive experience shows that a majority of patients react to quite a limited range of allergens (especially to feathers, house dust, horse dander and grass pollens), and almost identical "patterns of allergy" are found in hundreds of patients. (One curious pattern is found in young patients who develop asthma after having had infantile eczema. A majority of these show marked reactions to horse dander and to egg-white.) Allergens such as sheep's wool, rabbit fur and orris root rarely cause reactions; and when tests seem to show a large number of unusual reactions in a series of patients, it is a strong indication of lack of skill on the part of the person doing the tests.

Allergy to drugs (such as aspirin, phenobarbitone and phenolphthalein) is fairly common, but these drugs practically never cause a reaction when tested on the skin, and the only way to detect intolerance is to administer cautious doses orally.

Once the pattern of sensitivity has been found, it must be correlated with the history. For instance, if a patient who reacts to feathers, house dust and pollens has symptoms only during the early summer, the best results will usually be obtained by treating him with pollens only; whereas if his symptoms are perennial, the best treatment would be to give a mixture of these allergens. If he has perennial asthma and gross infective sinusitis or polyposis and reacts strongly to some allergens, it often transpires that the sinus disease is the dominant factor and that anti-allergic treatment is of no avail.

Elimination Diets.—In elimination diets, briefly, the patient tries in turn three types of diet: (i) All milk products are eliminated, and the patient lives on a plain, limited diet for five days. (ii) The patient takes only bread and milk products for five days. (iii) All wheat products are eliminated for five days. In this way all foodstuffs are in turn eliminated, and, if there is true food allergy, the patient improves rapidly during the application of one of these diets. Foods can then be added one at a time during the next few weeks and the offending food identified.

Summing Up.

The above investigations generally provide a satisfactory picture of the causes of the illness. One patient may present almost entirely an allergic problem, whereas the next may show no allergic clues but be found to have an antrum full of pus and be relieved by drainage, antibiotics and vaccines. In children particularly, allergy and infection often combine to precipitate attacks.

CHARLES SUTHERLAND,
Melbourne.

Medical Societies.

AUSTRALIAN ORTHOPÆDIC ASSOCIATION.

THE annual meeting of the Australian Orthopædic Association was held on September 9 to 12, 1953, at the Royal Society's Rooms, Hobart, DR. LENNOX G. TEECE, the President, in the chair.

Annual Report.

The Honorary Secretary's report for the preceding twelve months was received and adopted. The report was as follows:

I am pleased to report that the past year has been a very satisfactory one in every respect.

The last annual meeting was well attended, and at that meeting the magnificent gold emblem from the British Orthopædic Association was received.

Amendments to the Constitution—necessary for the election of a President-Elect—were carried at the annual meeting.

Owing to greatly increased costs, the meeting considered it necessary to increase the annual subscription to £2 2s.

Your executive committee held six meetings during the year, attendance by your office bearers being well maintained.

I regret to report that Dr. Denis Glissan, one of our foundation members and a most loyal advocate of this Association, has been sorely afflicted by illness, and our sympathy goes out to him and his wife at this time. During the year the Association has lost by death two members, in Dr. Alex Juett and Dr. William Herlihy.

Dr. H. C. Barry has resigned from the position of Registrar of Rare and Interesting Diseases, and Dr. H. R. T. Hodgkinson has been appointed to the position of Registrar.

Your committee has selected "Treatment of Pott's Fracture and a Study of End Results" as the subject for the Australian Orthopædic Association Prize Essay for 1954.

Since the last annual meeting the Australian Orthopædic Association has had the honour and pleasure of entertaining Dr. H. Kessler and Dr. J. Barr from the United States of America.

Membership now stands at 65 active members, 15 associate members, four honorary members and 10 corresponding members—a total of 94.

A. R. HAMILTON,
Honorary Secretary.

Election of Office Bearers.

The following office bearers were elected for the ensuing twelve months:

President: Dr. Lennox G. Teece.
President-Elect: Dr. Thomas King.
Vice-Presidents: Dr. D. W. L. Parker, Dr. J. R. S. Lahz, Dr. H. M. Hill.
Honorary Secretary: Dr. F. H. McC. Callow.
Honorary Treasurer: Dr. W. Hugh Smith.
Honorary Editorial Secretary: Dr. L. Macdonald.
Committee: Dr. D. P. Rowe, Dr. A. R. Hamilton, Dr. Warwick Stening, Dr. A. Watts.

Annual Dinner.

Dr. Lennox Teece, the President, welcomed the guests of the Association at the annual dinner, which was held at

Wrest Point Hotel. The guests included Dr. J. Bruce Hamilton (Royal Australasian College of Surgeons), Dr. Thomas Giblin (Tasmanian Branch of the British Medical Association), and the Editor of THE MEDICAL JOURNAL OF AUSTRALIA.

At the conclusion of the dinner Dr. Teece made a presentation to Dr. A. R. Hamilton, the retiring Honorary Secretary. Dr. Teece paid tribute to the great service which Dr. Hamilton had rendered to the Association over a period of sixteen years, from its inception as a small band of professional colleagues to its present mature status with a total membership of 80; its members were spread over all States of the Commonwealth, and it had a distinguished company of honorary and corresponding members. All the members felt that the smooth development of the Association, the repeated successes of the annual meetings from both the social and scientific aspects, and the happy cameraderie which existed among members, were in large measure due to Dr. Hamilton's organizing ability and whole-hearted enthusiasm.

President's Address.

DR. LENNOX TEECE took as the subject of his President's address, "Treatment of Relapsed, Resistant and Neglected Congenital Talipes Equino-Varus" (see page 845).

In the discussion on Dr. Teece's paper, numerous speakers agreed that where the deformity of *talipes equino-varus* was severe, the foot could never be restored to normal. Most agreed that division of soft parts should be employed when the condition was resistant to repeated manipulation, but the extensive Ober operation was criticized. Oblique osteotomy of the fibula was advocated as an effective method of correcting varus and equinus deformities due to narrowing of the tibio-fibular mortice. Most speakers preferred to wait till the patient had reached the age of twelve years before performing a bone resection on the tarsus to correct deformity. Transplantation of the *tibialis anticus* insertion to the outer side of the foot was regarded as beneficial where there was persistent weakness of the peroneal muscles.

Fractures of the Shaft of the Femur.

DR. W. D. STURROCK read a paaper entitled "Delayed Union and Non-Union in Fractures of the Shaft of the Femur" (see page 878).

DR. H. McC. CALLOW said that he had found the method described by Dr. Sturrock to be successful in gaining union in a high proportion of cases. He did not favour the Küntscher nail technique, and in some instances he thought the nail itself was a contributory factor to non-union. In the method described by Dr. Sturrock the essential point undoubtedly was the firm packing of the wide wedge in the bone with cancellous bone chips.

DR. D. W. L. PARKER spoke of the increasing incidence of fractures of the femoral shaft, due largely to the cult of the motor-cycle among young men. He thought that the twelve to sixteen week period was the time to make the decision whether operation must be performed. He agreed with Dr. Sturrock that interposition of soft tissue was a potent cause of non-union. Long post-operative immobilization was to be avoided.

DR. W. E. SWANEY said that with a view to providing internal fixation of such strength that post-operative immobilization was unnecessary, he was accustomed to use two plates in addition to the bone graft.

Dr. Sturrock, in reply, said that he hesitated to accept any form of internal fixation as adequate of itself to prevent strain at the site of fracture. He again stressed his opinion that interposition of muscle was a common cause of failure of adequate reduction by conservative means with resultant non-union. He had not found hæmorrhage troublesome in using a postero-lateral approach to the femur, nor had he found that this approach resulted in wasting of the *vastus lateralis*. On occasions he had met with suppuration occurring a long time after operation, but almost invariably this had been of an aseptic type because of defective materials.

Osteoporosis.

DR. E. F. WEST read a paper on "Osteoporosis" (see page 878).

DR. B. KEON-COHEN and DR. L. WOODLAND both drew attention to the frequent similarity of the X-ray pictures in multiple myelomatosis and senile osteoporosis; severe pain was more likely to occur in the former.

Bone Infection.

DR. R. HODGKINSON read a paper entitled "Bone Infection, its Problems and Attacks, with Special Mention of Streptokinase and Streptodornase" (see page 849).

Dr. Callow, in discussing Dr. Hodgkinson's paper, said that in the primary treatment of a compound fracture the elimination of sepsis was of the utmost importance. In that regard insufficient attention was often paid to gaining adequate skin cover. Tight suturing of a wound across a compound fracture was still a far too common occurrence in accident surgery. Unless easy apposition of the skin edges was possible, it was essential to make a relaxation incision, use a rotation flap or adopt some similar procedure. He also deprecated the use of a tourniquet in dealing with compound fractures. Their use invariably increased post-operative wound tension. He thought there was a definite place for the use of bone chips after a radical clean up of the chronically infected fracture—always with the proviso that skin cover was adequate. Also he had found that lumbar sympathectomy was frequently beneficial as a precursor to bone surgery in the treatment of the patient with a fracture of the tibia who had a long-standing infection and the cold, œdematous lower limb which often accompanied it.

DR. J. R. S. LAHZ drew attention to the ever-present danger of latent tetanus infection in all compound fractures; he said that antitetanic serum should be given pre-operatively in all such cases.

The Hip Joint in Cerebral Palsy.

DR. NEVILLE WILSON read a paper entitled "Change in the Hip Joint in Cerebral Palsy" (see page 852).

DAME JEAN MACNAMARA said that to understand the secondary changes which occurred in the hip joints of the spastic child it was necessary to appreciate the normal process in the healthy infant. The latter had *coxa valga* and drumstick femora; but his fat thighs and early attempts at standing with a wide base soon resulted in bone changes which made the hip joint architecturally secure. In the child with cerebral palsy adductor spasm prevented normal stresses and *coxa valga* persisted. Walking in such cases was liable to result in dislocation. She advocated the use of appliances (calipers with cross bar between the heels), in which the child was taught to stand for two to three hours daily before walking was attempted. Dame Jean Macnamara also said that the years had taught her that when dislocation had occurred in a spastic child, the displacement should be accepted, and that any attempt to treat it on the lines of an ordinary congenital dislocation was not in the child's best interest. Nor did she favour surgical attempts to deal with tight adductors, preferring to rely on constant passive stretching.

DR. CLAUDIA BURTON BRADLEY spoke of the classification of the cerebral palsies. She said that in her experience dislocation was a complication only in the "spastic" child.

In further discussion it was evident that there was a divergence of view as to the result of obturator neurectomy. One speaker had found that complete division of the nerve caused paralysis of the adductors and a loss of balance that made it almost impossible for the child to walk. However, another surgeon had found cases in which it was impossible to eliminate adductor spasm by prolonged stretching, and division of the obturator nerves in such cases had resulted in release of tension and an improvement in control.

Scoliosis.

DR. W. E. SWANEY read a paper entitled "Scoliosis" (see page 853).

DR. E. PRICE supported Dr. Swaney's insistence that it was necessary to classify the type of scoliosis as the primary essential to its treatment. As a working basis he thought there were four main types—compensatory, neurological, idiopathic and miscellaneous. The compensatory type remained stationary for years and treatment was unnecessary. Of the paralytic types, it was common knowledge that the high thoracic curves grew worse, and it was impossible to prevent deterioration even by cumbersome apparatus. In that type of case early operative fusion was advisable. In the treatment of lumbar curves apparatus was more successful, and a stiff lumbar section of the spine was a definite handicap. Those curves, too, would respond well to the correction of a turnbuckle jacket. Dr. Price said that over a period of ten years he had seen about 12 patients with infantile scoliosis (under the age of twelve months). They had been treated conservatively, with satisfactory results except in two cases. In one of the latter the condition had proved to be due to poliomyelitis, and fusion had subsequently

been carried out, and in the other treatment had been refused at an early date, and in a recent review a serious deformity was present.

Clinical Meeting.

A clinical meeting was held at the Royal Hobart Hospital.

Bone Tumours.

DR. T. HOGG, DR. D. W. L. PARKER and DR. A. MCL. MILLAR showed a series of patients suffering from bone tumours. The following conditions were present: (i) synovioma (three cases); (ii) three giant cell tumours occurring in unusual situations—(*a*) one in the sacrum, (*b*) one appearing subperiosteally in the shaft of the femur, with a recurrence in the soft tissues of the leg some years after the removal of the original tumour; (iii) multiple myelomata involving the spine (two cases), one of very slow growth, with a history of five years' duration, and one of rapid onset.

Slipped Epiphysis.

Dr. Hogg showed a series of patients suffering from slipped upper femoral epiphysis, treated by (*a*) nailing and (*b*) osteotomy.

Club Foot.

Dr. Millar showed a series of patients with club foot, treated by a modified Denis Browne method. He also showed a family in which four members out of eight had congenital dislocation of the hip and four had *talipes equino-varus*; two members had both conditions.

Arthroplasty, Fractures, and Extraarticular Arthrodesis of the Hip.

Dr. Parker showed a series of patients on whom arthroplasty of the hip by the Smith-Petersen vitallium cup method had been carried out, and as a contrast a series of patients treated by insertion of an acrylic femoral head.

Dr. Parker also showed a series of patients to illustrate the end results of treatment of severe multiple fractures of the upper and lower limbs.

Dr. Parker finally showed a series of patients on whom extraarticular arthrodesis of the hip had been carried out by the Van Gorder modification of the Trumble method.

MEDICAL DEFENCE SOCIETY OF QUEENSLAND.

ANNUAL MEETING.

THE fifty-second annual meeting of the Medical Defence Society of Queensland was held at British Medical Association House, 225 Wickham Terrace, Brisbane, on Wednesday, March 24, 1954, at 5 p.m., the President, DR. NEVILLE G. SUTTON, in the chair.

Annual Report.

The annual report for the year ended December 31, 1953, was adopted. The report is as follows:

The Council of the Medical Defence Society of Queensland has much pleasure in presenting the fifty-second annual report for the year ended December 31, 1953.

Membership.

The Society has now a membership of 659, as against 584 last year. During the year 114 new members were elected.

Obituary.

It is with much regret that we record the death of the following members: Dr. A. Gerrard Anderson, who was a members of the Council for many years, Dr. W. L. Fothergill, Dr. W. Kerr Scott, Dr. H. S. McLelland, Dr. Jean S. Stobo.

Office Bearers and Council, 1953.

The following office bearers were unanimously reelected by the Council: *President*, Dr. Neville G. Sutton; *Vice-President*, Dr. G. W. Macartney; *Honorary Treasurer*, Dr. T. V. Stubbs Brown; *Honorary Secretary*, Dr. R. G. Quinn; *Councillors*, Dr. T. R. Biggs, Dr. H. W. Horn, Dr. F. W. R. Lukin, Dr. H. Masel, Dr. Athol Quayle, Dr F. Garrett Scoles, Dr. J. G Wagner.

Dr. Neville G. Sutton, Dr. H. Masel and Dr. Athol Quayle, who retired in conformity with the by-laws, were reelected to the Council. Dr. H. Masel tendered his resignation as a member of the Council in October, for health reasons, which was accepted with regret. The vacancy was not filled.

Medico-Legal.

Proceedings have been resumed in two cases against members, which were referred to in the last annual report. In one of the cases no further developments have occurred, but a writ is likely to be served against the doctor in the second case.

During the current year three cases have been submitted to the Society. No developments have yet occurred in two of these cases, but action is proceeding in the third case.

General.

Accounts Work.—Following the resignation of Miss M. Heathwood, the British Medical Agency of Queensland Proprietary, Limited, who were responsible for this work, secured the services of Mrs. N. Davis, but subsequently found that working conditions had altered to such an extent, increase in membership *et cetera*, that it would be uneconomical to continue employing Mrs. Davis on a part-time basis under their control, and they relinquished the arrangement from June 30, 1953. Arrangements were then made to employ Mrs. Davis direct, to undertake the accounts work of the Society at a weekly remuneration.

Finance.

It will be shown from the balance sheet that the net surplus for the year ended December 31, 1953, amounted to £482 2s. 3d.

Some items of income and expenditure are as follows.

	£	s.	d.
Receipts—			
Annual subscriptions, Medical Defence Society of Queensland	352	4	9
Entrance fees	119	14	0
Subscriptions, indemnity insurance, Medical Society, Limited	3,711	5	9
Interest—			
Commonwealth Government Treasury Bonds and Inscribed Stock	252	9	9
Commonwealth Savings Bank	12	8	0
Expenditure—			
Amount remitted to Medical Protection Society	3,557	19	3
Secretarial and clerical assistance	204	0	0
Rent, postages, duty stamps, bank charges and sundries	24	19	6
Audit fee	13	13	0
Printing and stationery and filing cabinets	38	14	0
Federal income tax, year ended December 31, 1952	10	13	0

The total assets of the Society amount to £9242 5s. 2d.

An amount of £7,670 (nominal value) is invested in Commonwealth Government Inscribed Stock. Cost price was £7663 18s.

The current assets include bank balances amounting to £1549 0s. 6d.

NEVILLE G. SUTTON,
President.

Balance Sheet and Financial Statement.

The balance sheet and financial statement for the year ended December 31, 1953, was presented and adopted.

Election of Councillors.

The following councillors, who had retired in accordance with the by-laws, were reelected: Dr. H. W. Horn, Dr. T. V. Stubbs Brown, Dr. F. W. R. Lukin. Dr. W. J. Saxton was elected to fill a vacancy on the Council.

Election of Auditors.

Messrs. R. G. Groom and Company, Chartered Accountants (Australia), were reelected auditors for the ensuing year.

Membership.

It was resolved that it be a recommendation to Council that an approach be made to members of the British Medical Association who are not members of the Medical Defence Society of Queensland regarding membership.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

COOK'S FIRST VOYAGE.[1]

[April 13, 1769.]

AT this time we had very few men on the sick list and these had but slight complaints. The ship's company had in general been very healthy owing in a great measure to the sauerkraut, portable soup and malt: the two first were served by the people, the one on beef days and the other on banyan (meatless) days. Wort was made of the malt and at the discretion of the surgeon given to every man that had the least symptoms of scurvy upon him. By this means and the care and vigilance of Mr. Monkhouse the surgeon this disease was prevented from getting a footing in the ship. The sauerkraut the men at first would not eat it until I put in practice—a method I never once knew to fail with seamen—and this was to have some of it dressed every day for the cabin table and permitted all the officers without exception to make use of it and left it to the option of the men to take as much as they pleased or none at all: but this practice was not continued above a week before I found it necessary to put every one on board on an allowance: for such are the tempers and dispositions of seamen in general that whatever you give them out of the common way—although it be ever so much for their good—it will not go down and you will hear nothing but murmurings against the man who first invented it: but the moment they see their superiors set a value upon it, it becomes the first stuff in the world and the inventor an honest fellow.

Correspondence.

ANO-RECTAL COMPLICATIONS IN "MYCIN" THERAPY.

SIR: The ano-rectal complications in "mycin" therapy noted in "Current Comment" of May 8, 1954, can be easily prevented by gentian violet. One half-grain tablet taken twice a day is usually sufficient. The stools, of course, are stained by the dye.

Yours, etc.,

S. ROSE.

Flat 17 "Lenhurst",
33 Queen's Road,
Melbourne, S.C.2.
May 12, 1954.

TREATMENT OF THE COMMON WART BY X-RAY THERAPY.

SIR: It is with some diffidence that I wish to make a few warning remarks concerning an article, "Treatment of the Common Wart by X-Ray Therapy", by Alan Nelson, which appeared in the May 1 issue of THE MEDICAL JOURNAL OF AUSTRALIA. I do not wish to discourage a younger man in the use of a therapeutic modality which I strongly favour myself, but I feel that attention should be drawn to the possible sequelæ which may follow, in addition to the percentage of cures which may be expected (judged by my own experience) from the routine of treatment which he advocates. I personally have used X-ray therapy in the treatment of warts for close on thirty years, but have given up their use for these lesions, other than plantar warts, except in rare instances. Even for these, I do not employ X-ray therapy in older people for lesions situated over a bony prominence without much underlying soft tissue, and never employ a second course or single treatment to a wart which has failed to respond to the first treatment routine, because of necroses I have occasionally observed when this has been done, usually by two or more different doctors who have not been informed of previous X-radiation therapy.

The reason I no longer employ X rays or radium for the treatment of warts other than plantar warts is not that I consider them to be dangerous, but because of the frequency of occurrence of a marked telangiectasia which occurs in anything up to five to fifteen years after the treatment. These demarcated telangiectatic areas can be quite disfiguring, particularly on the fingers or hands of young females.

Also, among other routines I have employed, I have treated a number of plantar warts with 1000*r* of X rays (110 kilovolts, six milliamperes, 20 centimetres focus-skin distance, half-value layer 1·5 millimetres of aluminium) weekly to a total of 3000*r* in a fortnight after removal of surface keratin, and my percentage of cures with this routine has been well below 50%, even though 300*r* more than the routine (2700*r*) recommended by Dr. Nelson was given. Whereas, with a routine I have published in the *Australian Journal of Dermatology* (1951, 1: 20) I have achieved a cure rate of approximately 90% for plantar warts.

I might mention here that I am not unaware of the differences between plantar warts, mosaic warts, callosities, hard and neuro-vascular corns, for which (excluding plantar warts) X radiation is not considered to be efficient treatment.

One cannot help but wonder if the writer has inadvertently misquoted his cure rate (139 out of 140) in the same way as he has made the following statements: Under the heading "Technique" he states that "a dose of X-ray therapy (900*r*) was applied . . . the dose was repeated in a week and a fortnight later" (total time three weeks), and later under "Principles of Treatment" "(III) fractionation of dosage two weeks".

May I conclude by saying that no X-ray therapy routine can be properly assessed without an adequate observation time interval, which varies from five to fifteen years.

Yours, etc.,

J. C. BELISARIO.

143 Macquarie Street,
Sydney,
May 12, 1954.

INVESTIGATION OF BILIARY EXCRETION.

SIR: I hold a grant from the Royal Australasian College of Physicians to study liver function in man, particularly post-operative biliary excretion. The work is being carried out under the supervision of Dr. M. R. Lemberg, F.R.S. I should be grateful if any of your readers could refer cases of obstructive jaundice to the Unit of Clinical Investigation, the Royal North Shore Hospital of Sydney, to further this study.

Yours, etc.,

M. H. CASS.

The Royal North Shore Hospital of Sydney,
Crow's Nest,
New South Wales.
May 11, 1954.

TRAINING OF GENERAL PRACTITIONERS.

SIR: The Post-Graduate Committee in Medicine deserves credit for arranging the recent conference on the above subject. The discussion was stimulating, and, no doubt, will not be lost on the powers-that-be, who are charged with the all-important task of training doctors. Some sobering thoughts for reflection emerge therefrom. It is fashionable for Australians to claim superiority for their country's way of life, its educational methods and so on, too often without knowing enough about conditions overseas to make an intelligent comparison. And so it is with our doctors. It is claimed our general practitioners are the best in the world. No less an authority than Professor Dunlop supports the claim, and so, let us concede ourselves the honour! But can we lay unction to our souls on this score? I believe not. Traditionally, our medical schools follow English and Scottish methods, and it is assumed that the teaching standards are approximately the same. Few would claim we have a higher teaching standard; indeed, in recent years, the ridiculously overcrowded Faculty of Medicine at Sydney would make it well-nigh impossible to teach medical students as they should be taught. It can be assumed, however, that they get a reasonably good basic training. What, then, is the reason for the superiority of our graduates over others similarly trained? I believe it is due to an imponderable factor inherent in the Australian character. Given the same, or

[1] From the original in the Mitchell Library, Sydney.

even lesser, chance, he can excel all others in any field. Two great wars have thrown our manhood into competition, as it were, with the world in arms. By common consent, they were incomparable in battle, though we know their training was necessarily inadequate; indeed, by professional soldiering standards, it was woefully deficient. The same story can be told of the arts, of the theatre, of science and, notably, of sport especially. Our nurses, though none would claim superiority in their training, have gained for themselves an enviable name overseas, especially in the United States and in Canada. In the latter, they are in great demand. Whatever, then, this imponderable character-factor may be, call it initiative, practical application of principles or "know how", it does seem to make for superiority. Some would claim that access to hospitals makes the difference, but we know that a great number of general practitioners in small country areas, and also in large cities, have either no hospital amenities, or no access thereto, and have to rely on their own resources. But we must not be complacent and rest on our laurels. If our standard is high, we well know it can, and should be, a lot higher. *In meliora contende!* That is why the excellent work of the Post-Graduate Committee in Medicine, the work of F.O.C.L.A. (Federation of Country Local Associations) and, latterly, the College of General Practitioners, in their medical education programmes, must be vigorously supported. Our medical journals can help here. The greatest enemy of medical efficiency is apathy. The vast majority of doctors ignore the opportunities presented to them to learn their job and keep abreast of progress. A campaign to awaken them to the need for further medical education is required. It is common experience that the excellent post-graduate courses now available are extremely poorly patronized.

A final word about practical tuition for graduating doctors. The isolated experiment at Royal Melbourne Hospital, detailed by Dr. Ewen Downie, and lasting over twenty years, and the somewhat similar one at Newcastle Hospital, of over three years' duration, as explained by Dr. McCaffrey, are excellent in themselves, but a mere bagatelle in the over-all problem to be faced. Are they the optimum in this field and, if so, why are they ignored by the medical faculties in the respective universities? Nobody who sees the work of the new graduate (and who better is able to judge this than established practitioners who employ them?) doubts the deficiency in his training as regards practical work, more especially in obstetrics, and this could be fatal, were he left to his own resources in a remote area. A good case can be made out for a year's post-graduate apprenticeship to an approved general practitioner before full registration is granted.

Yours, etc.,

9 Park Road,
Bulli,
New South Wales.
BERTRAND A. COOK.

May 15, 1954.

DETERGENT INHALATION THERAPY.

SIR: Following a short article by Dr. Mervyn Smith and myself in the issue of THE MEDICAL JOURNAL OF AUSTRALIA, April 10, 1954, I have been asked for further details of the preparation of the aerosol detergent.

Cold drawn olive oil should be filled into an eight ounce bottle to a volume of six ounces. The bottle should be plugged with a cotton wool plug and autoclaved at 20 pounds for thirty minutes. The cork should be wrapped in paper and used to replace the cotton wool after the bottle has cooled. Add four cubic centimetres of triethanolamine in a sterile test tube by judging the volume as compared with four cubic centimetres of water. The triethanolamine is too viscous to pipette or draw up in a syringe. Shake the bottle well and allow to stand for twenty hours, when a brown layer will have formed at the bottom of the oil. Remove the oil into a sterile second eight ounce bottle plugged with cotton wool and having available a sterile autoclaved cork wrapped in paper. Sterile distilled water is added to the brown layer to a volume of six ounces and the bottle shaken well after replacing the cork. Frothing should occur immediately, indicating the lowering of surface tension of the water, and the detergent is ready for use. We have found that the extracted olive oil may be conserved for surgical use as emulsion and the supply exceeds that of detergent for all routine uses. It is best to use detergent within a week or two after making it up with sterile water. For batch production, however, just pour the oil off and leave the brown layer in the bottom of the bottle until subsequently required for use, and then add sterile water.

Add about one ounce of the detergent solution to the bottle of sterile olive oil, which has been extracted by the triethanolamine, and shake the bottle well to produce an emulsion. This is satisfactory for use immediately, but improves if kept for a time. The sterile olive oil emulsion is able to be used alone or as a vehicle for "Chloromycetin". It makes a good wound dressing, which is soaped off with detergent solution before making a fresh one. This provides 100% olive oil soap, which cleans the wound and appears to stimulate healing. Smells seem to disappear rapidly. A drop or two of oil of spike lavender in the emulsion seems to help very much, but is not often necessary. For skin toilet the emulsion has been used after methylated spirit to prevent drying and defatting.

To add "Chloromycetin" to the emulsion take one or two capsules of 250 milligrammes. Heat a pair of discarded artery forceps and allow to cool. A pull with the warm forceps will soften and take the end off. By compressing the sides of the capsule between the fingers the "Chloromycetin" powder will fall through the neck of the bottle into the emulsion. The bottle should be shaken well to distribute the "Chloromycetin" evenly throughout. The olive oil emulsion is slightly alkaline. It has not been found to interfere with the activity of the antibiotic, and facilitates prolonged contact with the tissues.

In order to prevent the confounding of the container with detergents of the industrial type, which are used for hospital cleaning and are sometimes very toxic, it is suggested that the label on each bottle bear the letters "T.E.O." (triethanolamine oleate) followed by the word "Inhalant".

Yours, etc.,

Pathology Department,
Repatriation General Hospital,
Concord,
New South Wales.
H. L. CARRUTHERS.

Undated.

Obituary.

JAMES HAROLD WILLMOTT LEADLEY.

DR. WARREN MURPHY has sent the following appreciation of the late Dr. James Harold Willmott Leadley.

James Harold Willmott Leadley died at Sydney in December last, at the age of fifty-six years. He was born in Lithgow, New South Wales, the son of the Reverend James Leadley, at that time Methodist minister of the town. After attending school at various country centres he entered Sydney Grammar School in 1911, at the age of fourteen years. His record at "Grammar" was a distinguished one, both scholastically and on the sporting field. He had the amazing performance in Great Public Schools athletics of winning the 100 yards championship in 1913, 1914 and 1915. In the 220 yards championship he was first in 1913 and 1914, and second in 1915. His 100 yards time in 1915 was 10·4 seconds, equalling the then Great Public Schools record. In the same year he created a Dunn Shield 200 yards record. He was naturally awarded his school colours in athletics in 1914 and 1915. On the academic side, he won the highly valued Wigram Allen Prize for mathematics, and at the Leaving Certificate of 1915 he was awarded a public exhibition, proceeding to the Faculty of Medicine in the University of Sydney.

Leadley's record as an undergraduate was again outstanding in both academic and sporting spheres. He won the G. S. Caird Scholarship Number 1 for first place in the fourth year. He was appointed prosector and later demonstrator in anatomy, and graduated in 1922 with second class honours. At the end of his third year he was one of a group of students who enlisted for active service, but the armistice was declared just prior to their embarkation. His athletic career was somewhat curtailed owing to the war years, but was none the less outstanding; he was never beaten in university or intervarsity sprints. Upon graduation he spent one year at the Royal Prince Alfred Hospital as a resident medical officer. In 1923 he proceeded to the Prince Henry Hospital where he remained for four years; during this time he gained an extensive surgical experience which was to prove valuable in his later career.

After a brief period of ten months at Armidale, he purchased the practice of Dr. William Wood at Bondi Beach, where he was to spend the remainder of his professional life. In 1926 he was appointed honorary surgeon to the

Coast Hospital, and he retained this position for five years until his resignation. Dr. Leadley had two trips abroad, once in 1936 for fourteen months and again in 1949 for nine months. On the first occasion he proceeded to the D.R.C.O.G. examination, which he passed.

During his long career in general practice he had many interests, the two outstanding of which were the War Memorial Hospital, Waverley, and Wesley College, University of Sydney. He was a councillor of Wesley from 1922 until the time of his death, having been associated with the College since his admission there on its opening in 1917. He was also a member of the Council of the War Memorial Hospital, Waverley, for many years. He was especially responsible for and justifiably proud of the first class operating theatres now in use at the hospital. He was the past president of the Eastern Suburbs Medical Association, within the British Medical Association, in whose affairs he always took a very keen interest. During World War II he organized a fund for the wives of eastern suburbs practitioners on active service. He was associated with Kambala School for many years as their medical officer. Of latter years he was a member of the Australian Golf Club.

In 1929 he married Miss Dorrie Downey, and there were three children of the marriage. His wife, his constant companion, was the greatest aid and comfort to him throughout his life.

OWEN FULTON ROFE.

DR. K. S. MILLINGEN, assisted by D.A., has sent the following appreciation of the late Dr. Owen Fulton Rofe.

To what nobler epithet can any doctor aspire than "he was loved by all his patients"? Such applies to Owen Rofe, whose passing bereaved many of a valued friend and counsellor, as well as a very fine doctor. Owen Fulton Rofe was born in Sydney, the son of the late Wyndham Rofe and a grandson of the late A. B. Shand, a noted legal personality in Sydney. He was educated at Scots College and the University of Sydney, graduating from the faculty of medicine in 1947. During his undergraduate days he took an active interest in the Sydney University Medical Society. He was for six months a resident medical officer at the Lismore Base Hospital, and in April, 1948, commenced as a resident medical officer at the Royal Hobart Hospital. He later served the hospital as clinical assistant and physician to the goitre clinic, and was distinguished for his great interest in people, for his careful detailed histories and for his sympathetic understanding of his patients; these qualities built up for him a large and successful practice as a physician. He owed much to Dr. Ralph Whishaw, and frequently spoke of his debt to him. His selfless nature made him very much more than a medical adviser to his patients, and the sincere grief felt by so many of them at his death is adequate testimony to the way in which Owen Rofe carried on the Hippocratic tradition.

Owen had many extramural interests and hobbies: gardening, carpentering, chess and a fondness for good literature, and he was a keen golf and tennis player. His greatest love, however, was music. He had studied the piano and 'cello from the age of fifteen years and won a Sydney Conservatorium Scholarship, which he only partly used during his student years. He played in the then New South Wales Symphony Orchestra and later was an enthusiastic member of chamber music groups meeting weekly among friends in Hobart.

In 1951 Owen married, and his wife shared his passion for music and literature. Her placidity, common sense and strength of character were of tremendous assistance to him. To his wife with her two young sons and to his mother his colleagues in Hobart would like to offer their sincere sympathy.

LUDWIK HIRSZFELD.

LUDWIK HIRSZFELD, who died on March 7, 1954, was born in Warsaw on August 5, 1884. He studied medicine in Würzburg and Berlin, obtaining his degree in 1907. In the years 1907 to 1911 he worked with Emil von Dungern in the Cancer Institute in Heidelberg and then in the Hygiene Institute in Zürich, where he obtained the degree of *Privat-Dozent* in 1914. From 1915 to 1920 he served as a volunteer in the Serbian Army, where he organized and led the Central Bacteriological Laboratory. In 1920 he returned to Poland where he became director of the Serum Institute and then vice-director and scientific leader of the Hygiene Institute in Warsaw. From 1931 he was professor of the medical and pharmaceutical faculty of the university in Warsaw. During the German occupation he was expelled from the Institute as a non-Aryan and interned in the ghetto of Warsaw. There he organized a bacteriological laboratory in the hospital, combated the typhus epidemic and participated as lecturer in the secret school of medicine. After the escape from the ghetto in 1942 he hid under a foreign name. In 1944 he was one of the main organizers of the university in Lublin, where he was professor of microbiology and prorector. In 1945 he arrived in Wroclaw, where as first dean he organized the faculty of medicine. He also took an active part in the organizing of the health service and of the scientific life in Poland. In the last years of his life he created in Wroclaw the Institute of Immunology and Experimental Therapy of the Polish Academy of Sciences, which after his death was renamed Ludwik Hirszfeld's Institute.

Ludwik Hirszfeld was a scientist whose work and discoveries were of first-class importance for biology and medicine. With von Dungern he discovered in 1911 the heredity of blood groups. With his wife, Hanna Hirszfeld, he described in 1918 basic serological differences in racial groups. He foresaw the possibility of serological conflict between mother and fœtus and its biological and social consequences. This hypothesis was confirmed after the discovery of the Rh group. In the last years of his life he was particularly concerned with the pathology of pregnancy and especially of habitual abortions. He demonstrated that the mechanism of these abortions frequently consisted in the incompatibility of the blood groups of mother and fœtus. He created the allergic theory of abortions and introduced treatment with antihistaminic drugs into this field. He discovered the paratyphus strain *Salmonella hirszfeldi*.

Hirszfeld was an honorary member of many scientific societies in Poland and abroad, including the Scientific Society in Charkov, the French Society of Allergists and the Academy of Sciences in New York. He was co-editor of many scientific journals in Poland and abroad.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Week-End Courses during June and July, 1954.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that the following week-end courses will be held.

Broken Hill.—On June 12 and 13 at the Broken Hill and District Hospital the course will be as follows: June 12: 10.30 a.m., "The Use of Hormones in Gynæcology", Dr. R. H. Macdonald; 11.30 a.m., "Modern Treatment of Arthritic Disease", Dr. Selwyn Nelson; 2 p.m., "Palliative Treatment in Carcinoma", Dr. R. M. Rawle; 3 p.m., "Early Diagnosis of Cancer of the Cervix", Dr. R. H. Macdonald; 4.15 p.m., "Common Neurological Disorders and Their Treatment", Dr. Selwyn Nelson. June 13: 10 a.m., "Some Surgical Conditions in and Around the Mouth", Dr. R. M. Rawle. The fee for attendance at the course will be £5 5s. Those wishing to attend are requested to communicate as soon as possible with Dr. F. Schlink, Honorary Secretary, Broken Hill Medical Association, 252 Mica Street, Broken Hill. Telephone, Broken Hill 865.

Katoomba.—On June 26 and 27 at the Carrington Hotel, Katoomba, the course will be as follows: June 26: 2 p.m., registration; 2.30 p.m., "Some Disorders of the Neonatal Period", Dr. S. E. L. Stening; 4 p.m., "Occlusive Vascular Disorders: Recent Advances in Surgical Treatment", Dr. F. F. Rundle. June 27: 10 a.m., "Problems of Hæmoptysis", Dr. A. G. McManis; 11.30 a.m., "Medical Emergencies in Childhood", Dr. S. E. L. Stening; 2.30 p.m., "The Diagnosis and Management of Thyroid Diseases", Dr. F. F. Rundle; 4 p.m., "Asthma", Dr. A. G. McManis. The fee for attendance is £3 3s. Those wishing to attend are requested to communicate as soon as possible with Dr. Nicholas Larkins, Honorary Secretary, Blue Mountains Medical Association, Katoomba Street, Katoomba. Telephone, Katoomba 111.

Wollongong.—On July 10 and 11 at the Wollongong District Hospital the course will be as follows: July 10: 2.15 p.m., "The Modern Treatment of Hypertension", Dr. Frank

Ritchie; 3.45 p.m., "The Management of Acute Intestinal Obstruction", Dr. V. M. Coppleson. July 11: 9.15 a.m., "Electrocardiographic Conference", Dr. Justin Markell; 10 a.m., panel discussion on "Diseases of the Liver and Biliary Tract", Dr. V. M. Coppleson, Dr. Frank Ritchie and Dr. Wallace Pullen; 11.30 a.m., "The Management of Diabetes in General Practice", Dr. W. Wilson Ingram. Fee for attendance is £3 3s. Those wishing to attend are requested to communicate as soon as possible with Dr. John Maude, Honorary Secretary, South Eastern Medical Association, Church Street, Wollongong. Telephones: B 1905 and B 1086.

Course for Diploma in Clinical Pathology.

A course suitable for candidates for the diploma in clinical pathology of the University of Sydney will begin on July 20, for a period of seven months. Those wishing to attend are asked to communicate as soon as possible with the Course Secretary, The Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney. Telephones: BU 5238, BW 7483. Telegraphic address: "Postgrad Sydney."

Course in Obstetrics and Gynæcology.

The Post-Graduate Committee in Medicine in the University of Sydney announces that a course in obstetrics and gynæcology will be conducted by the staff of The Women's Hospital, Crown Street, Sydney, in conjunction with the Royal College of Obstetricians and Gynæcologists, for one week from August 30 to September 3, 1954. The course will be limited to 15 post-graduate students in residence, and 10 attending as external students. Fees for attendance are £8 18s. 6d. (including board and residence) or £6 6s. (external attendance). Candidates should take up residence on Sunday afternoon, August 29. A detailed programme is available. Application should be made in writing to the Course Secretary, The Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney, stating whether it is for attendance as a resident or external student. Enrolment will be made in order of receipt of fees, and the list will be closed as soon as the required number of applications is received. Telephones: BU 5238, BW 7483. Telegraphic address: "Postgrad Sydney."

Week-End Course in Pædiatrics.

A week-end course in pædiatrics will be held at the Royal Alexandra Hospital for Children on Saturday and Sunday, September 4 and 5, 1954. The supervisor of the course will be Professor Lorimer Dods, Director of the Institute of Child Health. The fee for attendance is £3 3s. A detailed programme is available. Written application, enclosing remittance, should be forwarded to the Course Secretary, The Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney. Telephones: BU 5238, BW 7483. Telegraphic address: "Postgrad Sydney."

Medical Prizes.

THE SHORNEY PRIZE.

THE Shorney Prize, established for the purpose of perpetuating the memory of the late Herbert Frank Shorney, M.D., F.R.C.S., Lecturer in Ophthalmology in the University of Adelaide from 1926 to 1933, will be offered for the fifth time in 1955, and will be for work in diseases of the ear, nose and throat.

The relevant clauses of the Statute are as follows:

3. A post-graduate prize, to be called The Shorney Prize, of the value of £100, shall be awarded to the candidate who in the opinion of the examiners has made the most substantial contribution to knowledge in the subjects of ophthalmology or of diseases of the ear, nose and throat. The prize shall be offered alternately for work in ophthalmology and in diseases of the ear, nose and throat.

4. The recipient must be a graduate of an Australian university.

5. The material submitted for the prize may be either a thesis or published work in medical or scientific literature.

6. Each candidate must declare that the work described is his own.

7. The prize shall be offered for competition from time to time as the accumulations of the fund permit.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED MAY 15, 1954.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	5(4)	5(4)	..	..	..	..	..	..	10
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	1(1)	..	1	..	..	..	10	..	12
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	1	..	..	..	..	..	..	..	1
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	2	23(18)	5(5)	..	..	..	..	..	30
Diphtheria	6(6)	1(1)	5(1)	..	3(3)	..	..	..	15
Dysentery (Bacillary)	..	..	..	..	..	6(6)	..	..	6
Encephalitis	1	..	..	..	..	..	..	..	1
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	17(1)	10(3)	..	..	3(3)	..	..	..	30
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	3	..	..	..	..	..	3
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	6(5)	6(6)	2	..	..	1(1)	..	..	15
Ophthalmia	..	..	..	..	1	..	..	..	1
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	1(1)	..	..	..	1
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	12(6)	12(10)	1(1)	5(4)	2	..	..	1	33
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	..	8(6)	..	..	6(5)	..	..	..	14
Salmonella Infection	..	..	..	..	1(1)	..	..	..	1
Scarlet Fever	16(7)	32(18)	2(1)	3(3)	3(2)	..	..	..	56
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	1(1)	..	..	..	1
Trachoma	..	..	..	..	..	..	..	..	..
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	11(10)	24(12)	24(10)	8(4)	2(2)	3	1	..	73
Typhoid Fever	1(1)	..	..	..	..	1	..	..	2
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

8. The prize shall be offered at least twelve months before the last day for the receipt of applications.

9. The prize shall not be awarded on any occasion unless in the opinion of the examiners the material submitted is of sufficient merit.

Applications, accompanied by three copies of the evidence which the candidates wish to submit in support, must reach the undersigned not later than June 30, 1955.

MEDICAL WOMEN'S SOCIETY OF NEW SOUTH WALES PRIZE.

THE Medical Women's Society of New South Wales Prize for 1953 was won by Dr. Clair Isbister for her contribution entitled "A Clinical Study of the Draught Reflex in Human Lactation".

Royal Australasian College of Surgeons.

SIMS COMMONWEALTH TRAVELLING PROFESSOR, 1955.

ADVICE has been received from the Royal College of Surgeons of England that Professor R. I. Harris, of Toronto, has been appointed Sims Commonwealth Travelling Professor for 1955. Under the terms of his appointment, Professor Harris will visit Australia and New Zealand on dates to be announced in 1955. Professor Harris specializes in orthopædics, and until recently was Assistant Professor of Surgery at the University of Toronto.

The Sims Commonwealth Travelling Professorship is made possible as a result of a benefaction received by the Royal College of Surgeons of England from Sir Arthur Sims in November, 1946. In founding the professorship, Sir Arthur Sims desired that an annual appointment should be made, and that the professor should assist in the advancement of medical science, either by lecturing, teaching, investigating or engaging in research within the British Commonwealth.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Masters, Harold Elliott, M.B., B.S., 1952 (Univ. Sydney), 106 Manning Street, Taree, New South Wales.

Perendi, Serafima, provisionally registered in accordance with the provisions of Section 17 (1) (*c*) of the *Medical Practitioners Act*, 1938-1953, 142 Albert Road, Strathfield, New South Wales.

Derkatsch, Helene, provisionally registered in accordance with the provisions of Section 17 (1) (*c*) of the *Medical Practitioners Act*, 1938-1953, 112 Doncaster Avenue, Kensington, New South Wales.

Nickelburg, Tadeusz, provisionally registered in accordance with the provisions of Section 17 (1) (*c*) of the *Medical Practitioners Act*, 1938-1953, cnr. Bond Street and Marine Parade, Maroubra Bay, New South Wales.

Guyot, John Raymond Blee, M.B., B.S., 1952 (Univ. Sydney), 671 Elizabeth Street, Waterloo, New South Wales.

Law, David John, M.B., B.S., 1950 (Univ. Sydney), 122 Tower Street, Panania, New South Wales.

Corrigan, Alfred Brian, M.B., B.S., 1953 (Univ. Sydney), Otho Street, Inverell, New South Wales.

Madirazza, Spasoje, registered in accordance with the provisions of Section 17 (1) (*c*) of the *Medical Practitioners Act*, 1938-1953, 28 Railway Street, Petersham, New South Wales.

The undermentioned have been elected as members of the New South Wales Branch of the British Medical Association: Barclay, William Arthur, M.B., B.S., 1954 (Univ. Sydney); Edwards, Kenneth David Gilmore, M.B., B.S., 1953 (Univ. Sydney); Furness, Diana Nowlan, M.B., B.S., 1953 (Univ. Sydney); Lucas, Brian Goodwin, M.B., B.S., 1953 (Univ. Sydney); Miles, Derek Frazer, M.B., B.S., 1950 (Univ. Sydney); Mitchell, John Howard (Surgeon-Commander), M.B., B.Ch., 1937 (Univ. Dublin); Ziegler, Anna, registered in accordance with the provisions of Section 17 (1) (*c*) of the *Medical Practitioners Act*, 1938-1953.

Deaths.

THE following deaths have been announced:

PHIPPS.—Henry David Phipps, on May 18, 1954, at Ormond, Victoria.

MACK.—Joseph McDouall Mack, on May 20, 1954, at Cooma, New South Wales.

HARKER.—Alfred Edwin Harker, on May 20, 1954, at Wallsend, New South Wales.

EDWARDS.—Dudley Edwards, on May 23, 1954, at Melbourne.

Diary for the Month.

JUNE 8.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
JUNE 11.—Queensland Branch, B.M.A.: Council Meeting.
JUNE 14.—Victorian Branch, B.M.A.: Finance Subcommittee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Tasmania: Part-time specialist appointments for the north-west coast of Tasmania.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £5 *per annum* within Australia and the British Commonwealth of Nations, and £6 10s. *per annum* within America and foreign countries, payable in advance.